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## EXPERIMENTAL SILICOSIS: QUARTZ, SERICITE AND IRRITATING GASES\*

By W. D. ROBSON, M.B.,

*Schumacher, Ont.*,

DUDLEY A. IRWIN, M.B. AND EARL J. KING, PH.D.,

*Department of Medical Research, Banting Institute, University of Toronto,*

*Toronto*

IN connection with his duties as medical officer of the McIntyre-Porcupine Mine, one of us (W.D.R.) was struck by the fact that the incidence of silicosis was higher in men who worked underground than in those working in the crushing-houses of the various mines, in spite of the fact that the amount of dust was much greater in the crushing-houses than underground. On investigating, he was impressed by the number of underground men who came up suffering from headaches, and found that they had been working in a "gassy" atmosphere. Ninety per cent of the time lost by illness was due to respiratory conditions, especially colds and bronchitis. These facts suggested the possibility that the underground atmosphere, due to the noxious products of combustion from blasting and the slightly lowered oxygen and increased carbon-dioxide content, had of itself an injurious effect on lung tissue which in some way might accelerate the production of silicosis. Having satisfied himself that this condition was worth investigating, the matter was taken up with the management in September, 1932, and it was decided to approach Dr. F. G. Banting, who agreed that an experimental investigation should be carried out in the Department of Medical Research. In order to test the theory, it was decided to submit rabbits to daily exposures of a dusty atmosphere containing an appropriate concentration of noxious gas.

The noxious gases in gold mines consist mostly of oxides of nitrogen formed by the explosion of the dynamite; smaller quantities of hydrogen, methane and carbon monoxide also occur. Data on the concentration of oxides of nitrogen which might be expected in mines were obtained from a paper by Perrott, Babcock, Bitting and Jones,<sup>1</sup> in which the concentration of the gas was shown to range from 62 to 498 parts per million (p.p.m.) in mine drift air, 10 to 20 minutes after blasting had occurred. The average of all figures was 250 p.p.m. This corresponds to 2.5 parts per 10,000 of NO<sub>2</sub>. Sulphurous gases occur as a result of blasting in sulphide-containing rock, e.g., pyrites. Quantities of SO<sub>2</sub> ranging from 0.001 per cent to 0.09 per cent (0.1 to 9 parts per 10,000) were found by Gardner, Howell and Jones<sup>2</sup> in the atmosphere of mines due to the "gases from blasting in tunnels and metal-mine drifts". In Rambousek's standard work, "Industrial Poisoning", it is stated that 1 part in 10,000 of NO, NO<sub>2</sub> or SO<sub>2</sub> is definitely, although not acutely, harmful.

The presence of finely particulate quartz in the lung has long been held to be responsible for the production of the fibrous nodules of silicosis, and the experimental introduction of quartz dust into the lungs of animals has been shown by several workers (e.g., Gardner<sup>3</sup> and Kettle and Hilton<sup>4</sup>) to produce fibrotic lesions comparable with those found in the clinical condition. Jones<sup>5</sup> has recently cast some doubt on this

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belief, however, by his finding in silicotic lungs of large amounts of sericite—a potassium aluminium silicate of the muscovite and mica family. It is Jones' contention that silicosis occurs only in mines having a high sericite content in the rock, and he believes the silicotic nodules to be due to the presence of sericite rather than of quartz particles in the lung. In view of Jones' results, it was decided to expose animals to sericite dust as well as to silica dust.

The samples of dust used in these experiments were prepared by the Department of Mining Engineering of the University of Toronto, by prolonged grinding of the quartz and the sericite-containing schist in a steel ball mill until they were reduced to a very fine powder. The sericitic schist consisted of rock from the McIntyre-Porcupine Mine, hand-picked by their geologist, whose petrographic examination showed a large amount of sericite as well as quartz and some carbonates. The quartz used for dusting was obtained from the same source (hand-picked bull quartz), and assayed, chemically and petrographically, almost 100 per cent silica. Microscopic examination of these dusts showed particles ranging in size from  $30\ \mu$  down to those practically ultra-microscopic. The majority of the particles were under  $5\ \mu$ .

The nitric oxide gas was formed by means of nitric acid and metallic copper in a Kipp generator. This reaction leads to the production of NO which in contact with air immediately unites with O to form  $\text{NO}_2$ . The sulphur dioxide gas used was the standard commercial product compressed in a steel cylinder.

Three groups of 25 rabbits each were subjected to daily exposures of gas, gas plus silica dust, and gas plus sericite dust. A control group of animals exposed to silica dust without gas was omitted, as this work had already been done in the Department of Medical Research by Dr. G. C. Cameron<sup>6</sup> without producing silicosis, even in rabbits which survived as long as two years after being exposed to dust for a six-months' period.

The rabbits were exposed to dust and known concentrations of gas in three wooden chambers (4 by 3 by  $2\frac{1}{2}$  feet). Glass windows were placed in the sides of the chambers for observation of the animals. Compressed air was fed into the chambers at a measured rate, using as a gauge a water manometer which had previously been standardized against an air meter. The air was led directly into the box in the case of the rabbits receiving gas only, and in the case of the groups receiving silica and sericite through a stout-walled flask which contained a quantity of the finely powdered dust. The flask was attached to the side of the box so that its side-arm, inserted through a rubber stopper, delivered the dust-laden air into the interior of the chamber. The flask was agitated by means of an electric motor, so as to stir up the dust continuously. A concentration of dust corresponding on the average to 200 million particles per cu. ft. (8,000/c.c.) was maintained.

The noxious gases were supplied from a central apparatus arranged to deliver the  $\text{NO}_2$  and  $\text{SO}_2$  into the three chambers. From this apparatus the gas was delivered through a calibrated bubbling apparatus containing petroleum oil. The rate of flow of gas was so arranged that the desired concentration of gases in the chambers was obtained.

The rabbits were exposed to an atmosphere of nitric oxide 2: 10,000 and sulphur dioxide 1: 10,000 for 3 hours daily. This amount of gas was found to be too great to be tolerated by the rabbits, and several died after a few days' exposure. The con-

centration was accordingly lowered at the end of three weeks to one-half this amount, namely, nitric oxide 1: 10,000 and sulphur dioxide 1: 20,000, for 2 hours daily.

The intention was to kill the animals of each group at regular intervals, but they died of acute pneumonitis after periods varying from 2 days to 40 weeks. Fortunately, the deaths occurred at approximately the same rate in all three groups and at about the desired intervals.

#### PATHOLOGICAL FINDINGS

All but two of the animals ultimately died of acute pneumonitis, bronchial in type, despite the lowered concentration of gas and the shortened period of exposure. In practically all animals the pneumonic process was confined to patchy areas scattered throughout the lungs. The microscopic observations were made on the portions of lung not involved by pneumonitis.

The lungs were removed from the animals and immediately fixed by gentle distension with 10 per cent formosaline introduced through the trachea. Blocks from the upper and lower lobes of both lungs and a mediastinal lymphatic gland were sectioned in all animals. The tissues were dehydrated in alcohols of increasing concentration, cleared in xylol, embedded and cut in paraffin. The sections from the dusted animals were mounted serially in sets of three: the first was incinerated; the second was stained with haematoxylin and eosin; and the third was incinerated and treated with concentrated hydrochloric acid to remove the non-siliceous ash. The sections from the rabbits exposed to gas alone were stained but not incinerated. Special fibrous tissue stains were used on selected sections.

1. *Animals exposed to gas.*—The gross appearance of the lungs of the rabbits exposed to gas was not remarkable, except for a marked congestion of the blood vessels and the patchy areas of pneumonitis mentioned previously.

On microscopic examination, widespread changes of the bronchial epithelium were seen in all animals exposed for periods longer than two weeks. This was evidenced by degeneration and desquamation (Fig. 1) of the epithelial cells associated with occasional areas of hyperplasia. Cilia could not be seen on the majority of these degenerating cells. Degeneration and desquamation of the bronchiolar epithelium were only occasionally seen. These cells showed varying degrees of flattening, which at times was pavement-like and stratified, and was more marked in animals exposed to gas for long

periods. The flattened cells were not ciliated. The walls of the bronchial tree constantly showed a lymphocytic infiltration (Fig. 1) that varied in degree in different animals. The severity of this infiltration did not indicate the length of gas exposure. The only change observed in the perivascular and peribronchial lymphatic spaces and aggregations and mediastinal lymphatic glands was slight oedema.

The alveoli in some areas appeared normal—a thin wall on which were occasional endothelial cells. In other areas there was a thickening of the alveolar walls accompanied by a marked endothelial proliferation. This endothelial proliferation was evidenced in several ways: (1) by the presence of many endothelial cells in the alveolar exudate (Fig. 2); (2) by tuft-like aggregations of endothelial cells protruding into the alveolar spaces (Fig. 3); (3) by a complete lining of the alveolar spaces with a single layer of endothelial cells (Fig. 4). In such alveoli there were occasional local protrusions of the thickened wall into the alveolar spaces (Fig. 4) which almost obliterated them. A slight endothelial proliferation was seen occasionally in animals exposed to gas as early as the third day,

but was more widespread and marked in those animals gassed for longer periods.

*2. Animals exposed to gas plus sericite dust.*—The gross appearance of the lungs of these animals was much the same as in those exposed to gas alone. Small greenish areas (sericite) were seen under the pleura. The cut surface of the lung showed similar areas scattered in an irregular manner throughout the substance. The patchy collections of sericite dust were distributed uniformly throughout all lobes of the lung, were not concentrated under the pleural surface, and did not bear any constant relationship to the bronchial tree.

The microscopic picture was essentially the same as that seen in the animals exposed to gas alone, except for the presence of the sericite dust. Many areas were seen, corresponding to the greenish patches in the gross, in which large numbers of endothelial cells containing sericite dust were present in the alveolar spaces (Figs. 5 and 6). These cells varied in size (Fig. 6), but were circular in shape, regular in outline, and their nuclei stained well. An occasional degenerated dust cell was seen, but the great majority showed no evidence of degeneration.

TABLE I.

TABULATION OF THE PATHOLOGICAL FINDINGS IN RABBITS SELECTED FROM THE SILICA+GAS GROUP

Tag No.	Duration Gas+SiO <sub>2</sub>	Bronchial Tree			Vasc. Lym. Agg.	Alveolar			Fibrosis			Microinc. of lung Amt. Sil. Mall.
		Epith.	Wall	Lym. Agg.		Wall	Endo.	Exud.	Alveolar	Lym. Agg.	Lym. Gld.	
49	3 wks.	degen. and desquam.	mod. infil.	×	×	slight thick- ening	slight endo. prolif.	mod. endo.	×	×	×	×
40	9 wks.	flattening, marked degen. and desquam.	marked infil.	slight œdema	×	mod. diffuse thick- ening	mod. endo. prolif.	marked diffuse endo.	×	×	×	mod.
34	10 wks.	marked degen. and desquam.	marked infil.	×	×	mod. diffuse thick- ening	areas of mod. endo. prolif.	marked diffuse endo.	occasional early nodules	×	×	mod.
46	14 wks.	desquam. and flattening	marked infil.	×	×	diffuse thick- ening	diffuse endo. prolif.	marked endo.	early nodules	early nodules	×	mod.
36	21 wks.	mod. flattening and degen.	mod. infil.	slightly enlarged	×	diffuse thick- ening	marked prolif.	marked endo.	occasional early nodules	occasional early nodules	early diffuse fibrosis	mod.
37	40 wks.	marked flattening with degen. and desquam.	mod. infil.	increased in number and size	×	marked diffuse thick- ening	marked diffuse endo. hyper.	marked endo.	scattered well formed nodules	occasional SiO <sub>2</sub> nodules	marked diffuse fibrosis	marked

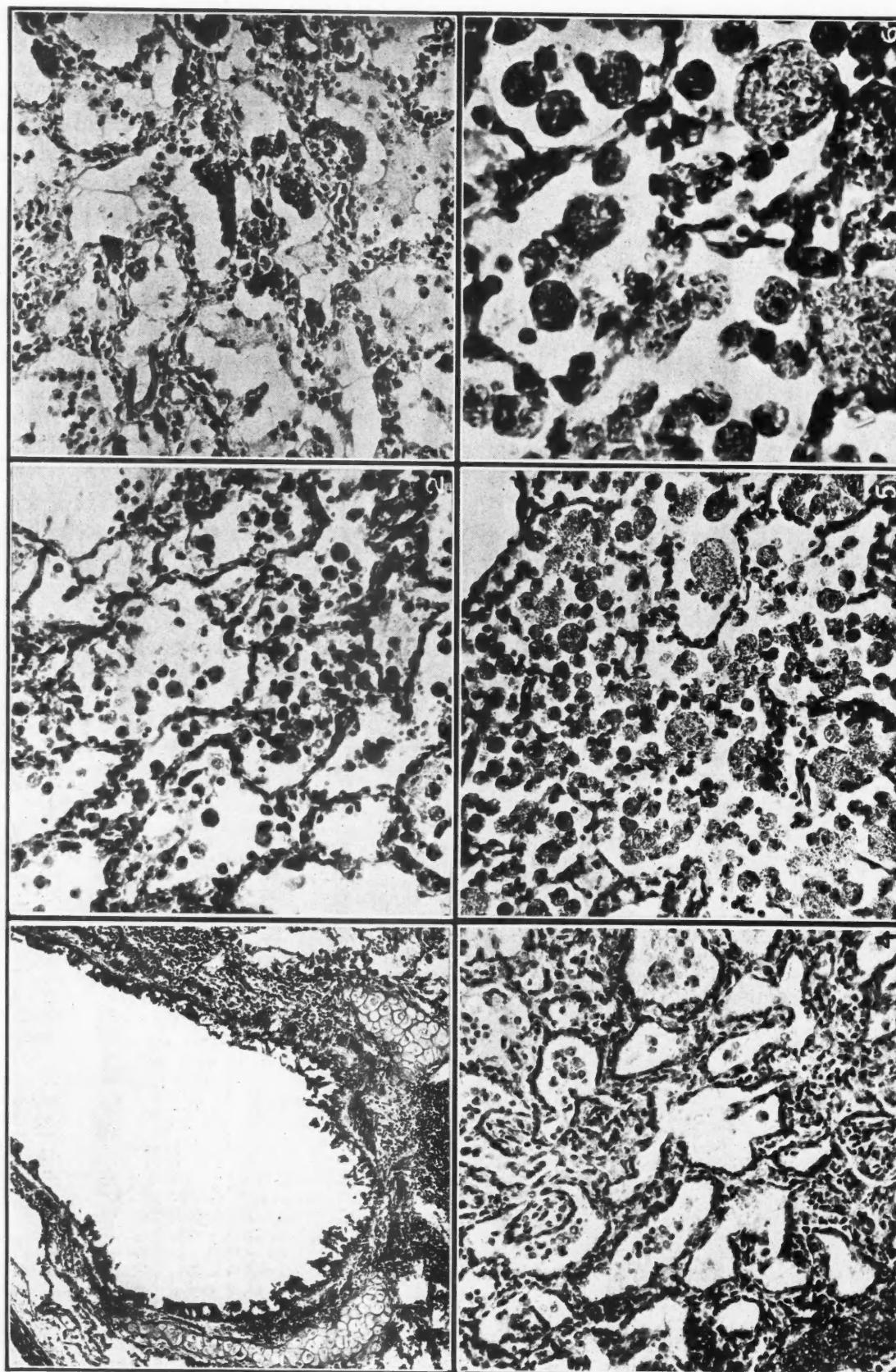


FIG. 1.—Gas rabbit. Small bronchus showing degeneration and desquamation of epithelium. L.P. FIG. 2.—Gas rabbit. Typical endothelial cell exudate in alveolar spaces. H.P. FIG. 3.—Gas. Tuft-like proliferation of alveolar endothelial cells. L.P. FIG. 4.—Gas. Marked thickening of alveolar walls and alveoli, completely lined by endothelial cells. Note ingrowth of walls into alveolar spaces. L.P. FIG. 5.—Gas and sericite, 30 weeks. Showing many dust cells in the alveoli. Note lack of any fibrous reaction. L.P. FIG. 6.—High power of Fig. 5.

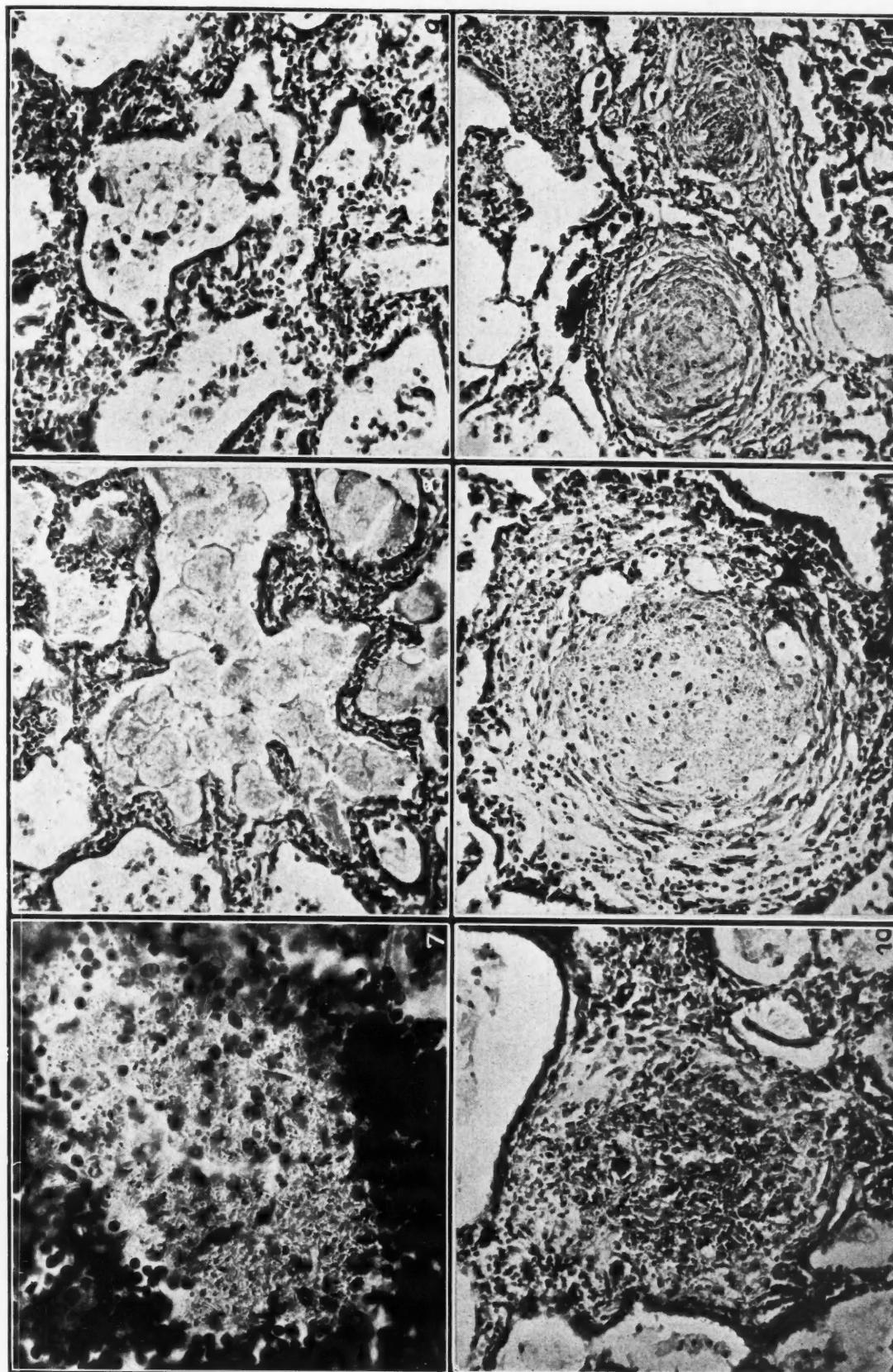


FIG. 7.—Gas and sericite, 20 weeks. Sericite dust cells in lymphatic gland. Note absence of any fibrosis. H.P. FIG. 8.—Gas and silica. Degenerated dust cells in alveolar spaces. Note thickened alveolar walls. H.P. FIG. 9.—Gas and silica. Invasion of wandering cells between degenerated dust cells with increased thickening of the alveolar walls. H.P. FIG. 10.—Gas and silica. Early stage of alveolar nodule. H.P. FIG. 11.—Gas and silica. Alveolar nodule showing whorl formation. H.P. FIG. 12.—Gas and silica, 14 weeks. Group of alveolar nodules. L.P.

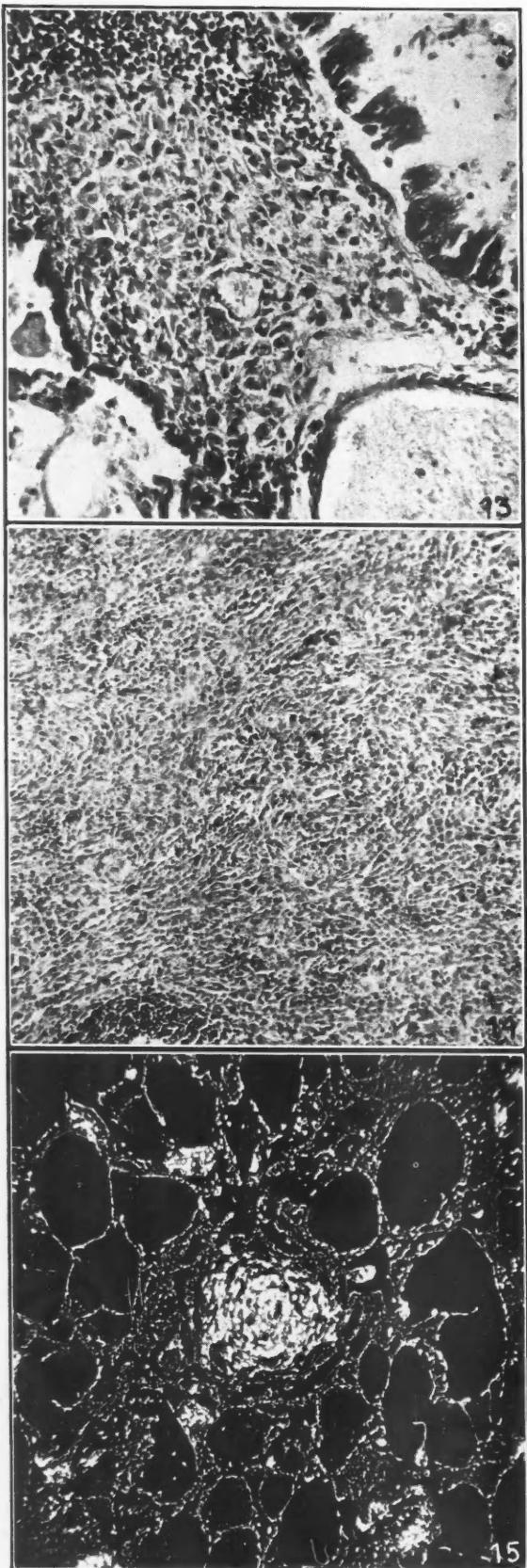


FIG. 13.—Gas and silica. Early fibrosis in peribronchial lymphatic aggregation. H.P. FIG. 14.—Gas and silica, 40 weeks. Diffuse fibrosis in lymphatic gland. L.P. FIG. 15.—Gas and silica. Incinerated section showing an alveolar nodule. The white ash in the centre of the nodule is siliceous material. H.P.

In these areas the number of cells contained within an alveolar space varied considerably. Some alveoli were packed with them, while others contained only a few. There was apparently no relationship between the presence of these cells and the thickening of the alveolar walls, as thickened areas frequently did not contain any dust cells and the walls of dust-containing alveoli were frequently not thickened. The lung tissue lying between these dust cell aggregates usually did not contain any dust cells. A few dust-containing cells similar to those seen in the alveolar spaces were usually present in the bronchial mucus. The peribronchial and peri-vascular lymphatic aggregations of those animals dusted for periods greater than a month usually contained a few dust-laden cells. Animals dusted for periods greater than two months usually showed similar cells in the mediastinal lymphatic glands (Fig. 7). Microincineration showed that practically all the dust in these lungs was present in phagocytic cells lying in the alveolar spaces. In all the animals of this series there was no evidence of fibrosis in the alveolar spaces, the lymphatic spaces and aggregations, or the mediastinal lymphatic glands associated with the sericitic schist dust.

*3. Animals exposed to gas plus silica.*—The gross appearance of the uncut lungs of the rabbits exposed to gas and silica was essentially the same as in those exposed to gas alone. The cut surface of the lungs of those animals exposed for periods of greater than fourteen weeks showed small firm greyish-white nodules scattered throughout the lung tissue. These nodules were scattered irregularly through all the lobes and did not appear to have any characteristic distribution. The mediastinal lymphatic glands of those animals dusted fourteen weeks or longer were enlarged to a varying degree. Some were several times the usual size. The cut surface of such glands revealed firm greyish nodules similar to those seen in the lung tissue.

Microscopically, the bronchial epithelium showed a degeneration and desquamation similar, but more marked, to that seen in the animals exposed to gas alone or to gas plus sericite dust. The bronchiolar epithelium showed a flattening of the cells that was more extensive and marked than the corresponding flattening seen in those animals of the other groups. The walls of the bronchial tree were infiltrated with lymphocytes in a diffuse manner. The alveolar walls of most

animals of this group were thickened. This thickening was due to the lining of the alveoli by a single layer of endothelial cells, the presence of oedema and a few lymphocytes, the engorgement of the alveolar capillaries, and to some extent by an increase in the number of reticular fibres. The degree of diffuseness of the alveolar wall thickening more or less paralleled the period of exposure to gas and silica dust, and was more marked in these animals than in those exposed to gas alone or to gas and sericite dust.

There were many dust cells in the alveolar spaces. Some of these cells were regular in outline, stained well, and doubly refractive particles could be seen in their cytoplasm. Other cells seen in the alveolar spaces were obviously degenerated (Fig. 8), as they appeared swollen, their outlines were irregular, no nuclei could be seen, and they had taken on a ghost-like appearance. These cells contained little, if any, doubly refractive material, but by incineration and acid treatment of their ash they could be shown to contain large amounts of siliceous material. The number of degenerated dust cells increased numerically and relatively with increasing periods of exposure to gas and silica dust. In animals so exposed for long periods practically all the dust cells were degenerated. The greyish nodules seen in the gross corresponded microscopically to areas of alveolar tissue that had taken on a nodular formation. These nodules usually presented a small central necrotic core about which proliferating fibroblasts were arranged in a whorl-like manner (Fig. 11). Many reticular fibres were seen associated with the fibroblasts and had the same arrangement. These nodules varied in size and occurred either singly (Fig. 11) or in small groups (Fig. 12). Acid-treated incinerated sections showed these nodules to contain a relatively large amount of siliceous material (Fig. 15) concentrated towards the centre of the nodule. These nodules were seen in all animals of this group dusted for a period of 10 weeks or more, and their numbers increased with the period of exposure. The development of these alveolar siliceous nodules could be traced, commencing with the incarceration of numbers of degenerated silica-laden phagocytes in an alveolar space (Fig. 8), followed by a thickening of the surrounding alveolar wall (Fig. 9) to the extent of the complete enveloping of the group of dust

cells (Fig. 10). Active proliferation of the reticulum of the alveolar wall then took place to form the nodule. The peribronchial and perivascular lymphatic spaces did not appear to be thickened. The lymphatic aggregations showed areas of varying size (Fig. 13), composed of proliferating fibroblasts and an increased number of reticular fibres. These fibrous areas, when incinerated, were seen to contain large amounts of siliceous material. The number and size of these areas increased with the length of exposure to gas and silica dust. These lesions were seen in all animals of this group exposed for periods of 13 weeks or more.

The lymphatic glands of the mediastinum showed areas of fibrosis similar to those seen in the lymphatic aggregation. These areas varied in size from those composed of a few cells to confluent areas (Fig. 14) that occupied most of the gland. The discrete areas were spherical and had a whorled appearance. They were composed of fibroblasts and a greatly increased reticulum, though occasional lymphocytes were present. The reticulum, when stained with silver, presented for the most part a matting of fine black fibres, though in the larger fibrotic areas the fibres were coarse and stained the same as the fibres seen in the capsule of the gland. These lesions were present in practically all animals exposed to gas and silica dust for periods greater than 13 weeks. Animals similarly exposed for periods of 10 to 13 weeks showed fibrotic areas in the alveoli and lymphatic aggregations, but no fibrotic areas were seen in the lymphatic glands of these animals.

#### DISCUSSION

The addition of noxious gases to the atmosphere breathed by the animals used in this investigation appeared definitely to lower their resistance to pulmonary infection. Acute pneumonitis was the immediate cause of death in the seventy-five rabbits used, with the exception of two animals that were killed after an exposure of forty weeks to gas and sericite dust. This high mortality was not due to epidemic pneumonia as the animals of all groups died at varying intervals, and death from pneumonia was uncommon in the other experimental animals housed in the same animal quarters during the corresponding period. The presence of patchy areas of pneumonia in the lungs of these animals added to the difficulties of the microscopic

pathological findings. In all animals there was plenty of lung tissue not involved by pneumonitis on which observations could be made as to the lesions produced by the gas and dusts. The widespread damage to the bronchial tree and the alveoli was not confined to the areas of pneumonitis and was interpreted as being due to the effect of the gas.

In the animals exposed to gas alone, the epithelium of the bronchial tree showed diffuse changes. The epithelium of the bronchi showed much evidence of degeneration and desquamation. The shape of the ciliated epithelial cells of most bronchioles showed varying degrees of alteration, which varied from a slight flattening to marked flattening with stratification of the cells. It was difficult to interpret the amount of damage done by the gas to the cilia of the bronchial tree. The damage to the ciliary mechanism must have been extensive, however, since few cilia could be seen on the degenerated epithelial cells of the bronchi and the flattened bronchiolar epithelial cells were not ciliated. The marked proliferation of the alveolar endothelial cells and the thickening of the alveolar walls were interpreted as being due to the irritating action of the gas. It would have been interesting, if these animals had survived for longer periods, to see if the alveolar wall thickening might have progressed to obliteration of the air spaces and fibrosis in the absence of dust.

In the group of animals exposed to gas and sericite dust, the dust was present for the most part in alveolar phagocytes, but also to a slight extent in the lymphatic aggregations and mediastinal lymphatic glands. The distribution of the sericite was very patchy in all animals. This was in contrast to the diffuse distribution of the silica found in the quartz-dusted animals. The apparent "health" of the alveolar phagocytes containing large numbers of sericite dust particles and the absence of any fibrotic response to their presence, indicate a low degree of toxicity of this dust. This absence of fibrous reaction is still more remarkable in view of the fact that the ground sericite schist used for dusting contained a considerable amount of free quartz.

In the group of rabbits exposed to gas and silica dust the siliceous material was distributed diffusely throughout the lung, a high percentage being contained in alveolar phagocytes. The microscopic examination of the amount and dis-

tribution of the siliceous fibrosis was indicative of the duration of exposure to gas and silica dust. Animals exposed to gas and silica for periods of less than ten weeks did not show any areas of siliceous fibrosis, though much silica was present in the lungs. Animals exposed for 10 weeks showed alveolar fibrotic nodules only, none being observed in the lymphatic aggregations or glands. Animals similarly exposed from ten to thirteen weeks showed areas of siliceous fibrosis in the lymphatic aggregations in addition to the alveolar nodules, but no fibrosis in the mediastinal lymphatic glands. All animals exposed for periods of thirteen weeks or more showed siliceous nodules in the alveoli and lymphatic aggregations and glands, with the exception of one rabbit that did not show any lymphatic gland fibrosis. This primary alveolar fibrosis with secondary lymphatic fibrosis is the reverse of the commonly accepted order of fibrosis in chronic pulmonary silicosis. On this account, and because of the rapid rate of development, the silicosis in the experimental rabbits is considered to be acute. (Gardner,<sup>7</sup> Chapman,<sup>8</sup> Kessler,<sup>9</sup> etc., have described "acute" silicosis in human beings).

The absence of silica-containing dust cells in the pulmonary lymphatic spaces, aggregations, and glands of these rabbits is in contrast with what obtains in sericite-dusted animals and the usual findings in human silicotic lungs. Despite the absence of such cells, many fibrotic areas containing much siliceous material were present in the lymphatic aggregations and glands. In these areas only very occasional doubly refractive particles could be seen, though in such areas large amounts of silica were present, as could be demonstrated by microincineration. Because of its invisibility in transmitted light and the lack of doubly refractive properties, this occult silica must have been present in a hydrated state. It is difficult to explain the presence of silica in these lymphatic fibrotic areas on account of the absence of dust-laden phagocytes from such areas. It is improbable that the silica was transported from the alveoli to these fibrotic areas by phagocytic cells, since no sign was seen of dust cells — intact or degenerated. It is probable that the silica which reached them consisted of very fine particles that had escaped phagocytosis in the alveoli and were carried in suspension in the lymph to the lymphatic aggregates and glands.

## CONCLUSIONS

1. Exposure of rabbits to dilute irritating gases ( $\text{NO}_2$  and  $\text{SO}_2$ ) produced degenerative lesions in the lungs and predisposed to pneumonitis.

2. Exposure of rabbits to dilute irritating gases combined with sericite dust did not produce fibrotic changes in the lungs in an exposure of forty weeks.

3. Exposure of rabbits to dilute irritating gases combined with silica dust gave rise in periods of thirteen weeks or more, to an acute pulmonary silicosis, characterized by typical siliceous fibrotic nodules first in the alveoli, secondly, in the lymphatic aggregations, and, thirdly, in the lymphatic glands.

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## SILICA DUST\*

BY W. R. FRANKS,

*Department of Medical Research, Banting Institute, University of Toronto,*

*Toronto*

SILICOSIS is an insidious type of poisoning. The toxic silica gains entrance to the body by being inhaled as dust particles which are deposited in the lung. Once the material has settled out on the lung surface it may either be phagocytosed *in situ* by the wandering dust cells, or it may be wafted up by the cilia of the bronchial tree and be swallowed into the gastrointestinal tract. No matter what the pathway, the net result is the accumulation of the dust-laden cells in the lung tissue. Clinical silicosis is thus primarily a pulmonary disease, and metastasis to other organs is the exception. The cause of silicosis then lies in the inhaled silica which is retained in the lung. Any factor which will modify the life-history of the siliceous atmosphere from the time of its formation to the lodging of the material in the tissues will modify the incidence of the disease. Silicosis should be preventable.

Silicon compounds may reach the lung either in a gaseous state or as dust. Gaseous silicates are known to exist, such as the silicon hydrides

and silicon tetrachloride (B.P. 57.5), but little information is available as to their possible occurrence in industrial atmospheres. The hydride is insoluble, whereas the tetrachloride rapidly breaks down in the presence of moisture into silica and hydrochloric acid. This reaction was used during the war to produce white smoke screens.

The relation of such gaseous silicates to clinical silicosis has yet to be investigated. The fact remains that experimental silicosis has been produced by the inhalation of particulate silica. In order that a silica particle may enter the lung tissue it must be of a certain size. (1) It must be small enough to persist in the atmosphere and be inhaled; particles larger than 10 microns settle rapidly. (2) It must be large enough to be precipitated in the alveoli during its sojourn there. Mavrogordato<sup>1</sup> places this minimal size at one-quarter of a micron in diameter. (3) It must be of a size that, once precipitated, it can be phagocytosed by the body cells.

By tissue culture we find that dust cells do not take up particles greater than 6 microns in diameter. The dangerous fraction of a silica

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dust, therefore, is that composed of particles from one-quarter to 6 microns in diameter, *i.e.*, of the order of size of common bacteria.

The size of a silica particle will depend upon many factors, chief of which are the following: (1) the energy expended when the dust is formed; thus blasting dust is finer than that formed by machines; (2) the age of the dusty atmosphere or aerosol; the particles tend to aggregate with time. Whytlaw-Gray<sup>2</sup> states that "all aerosols during the first stage of their life-history contain a relatively large proportion of matter either in the molecular state or as amicroscopic particles". Within half an hour of suspension in air, however, he found this material had aggregated to form microscopically visible particles. The aggregation is more rapid, the finer the particles, and is influenced by many factors, including temperature, humidity, pressure and ionization of the gas phase. Brownian movement plays its part here, especially in particles less than one micron in size. (3) The mass of the particle may be increased by the condensation of water upon it. With neutral particles, the smaller they are, the less liable they are to take up water. If, however, the particle is electrically charged this effect will be counteracted. Water will tend to condense even on the smallest particles. The minute silica fragment in the droplet then behaves as a larger one. Density is, of course, another factor influencing the settling out of a particle. The effective specific gravity of the silica particle is not fixed. By adsorption of gases on the surface a particle may greatly reduce its effective density. Although the aggregate has an increased mass, the particle moving with its "retinue" of adsorbed gas molecules offers more resistance. Upon a similar decrease in effective density depends most of the metal recovery in this country by the flotation process.

These particles with their adsorbed films of gas may still form loose aggregates. In this connection, Köhlschütter and Tüscher<sup>3</sup> studied the material of a silica smoke formed in an electric arc. The material possessed a low density and evidently consisted of loose aggregates. On treatment with water or dilute alkali this underwent a peptization to form a colloidal solution.

Granted that the dust persists to be inhaled, it must be deposited in the lung to be dangerous. Drinker and his associates<sup>4</sup> found a retention

on inhalation of 55 per cent of marble dust varying in size from 0.3 to 6 microns in diameter. Brown,<sup>5</sup> in a later study, found this retention increased as the dust became more dilute.

Some of the factors concerned in the deposition of the silica are as follows. (1) The settling effect due to gravity or mass attraction. This is probably considerable, since the distance to settle in the alveoli of the lung is small. The average time allowed for settling is roughly equal to

$$\frac{\text{Supplemental + Residual Air}}{(\text{Tidal - Dead Air}) \times \text{Respiration Rate per Minute}}$$

which is of the order of one-half minute. The settling effect is probably increased by the cooler dust particle taking up water in the lung. (2) The impinging action of the dust as it passes down the irregularities of the air ducts. In both this and the foregoing the larger particles are most concerned, but the centrifugal action of the air-flow down the passages probably deposits most of the large material on the ciliated epithelium before it reaches the alveoli. (3) Electrical attraction between the dust particles and the alveolar wall also plays its part. The charge on the lung wall probably changes sign with the cardiac and respiratory cycle, so that at one phase in the cycle the charged particle is bound to be attracted. Thus Yaglow, Benjamin and Brandt<sup>6</sup> found that expired air was devoid of small ions.

Opposing the deposition of the particle is the heat radiation from the lung wall. Radiant energy will cause a particle to move away from the region of greater radiation toward the less. Thus dust particles tend to settle on cold bodies. An attempt to use this principle for dust abatement has been made in South Africa. An example of it is seen in the deposit of dust on the ceiling of rooms. The dust accumulates on the colder areas of less radiation between the laths. Such a radiation gradient exists at the warm lung surface. The diffusion of water vapour from the alveolar wall aids this effect. Gibbs suggests that this is the determining factor in the non-deposition of material under one-quarter of a micron in diameter.

Once the silica is taken into the body cells it begins to exert its toxic action. In view of its slight solubility the determining factor in the reaction must be one of surface rather than of mass. Thus the course of uncomplicated

silicosis, once it is established, is not greatly affected by removing the man from the dusty air. At present the non-complicated silicotic is not removed from his occupation. The dangerousness of a silica dust is, therefore, proportional to the total surface of the particles of a size which may be deposited in the lung.

The methods used in the past for measuring the dustiness of the air have been either gravimetric or chemical, both of which depend upon the mass of the offending dust. Dust is also measured by counting the number of particles in a unit volume. The method most widely used in the mining industry, both here and in South Africa, is the konimeter count. The konimeter samples probably recover by impingement as great a proportion of the material as the lung retains. It is also very convenient to use. The slides may be treated by the South African method of hydrochloric acid and heat to remove all but the siliceous material. Neither the count nor the gravimetric method estimate the real dangerousness of the dust, which can only be done by estimating the surface. The dust spots from the impinged volume of air are estimated under the dark field microscope by counting the number of particles in two sectors at right angles to each other across the field. The results are expressed as particles per c.c. The repeated counting of such fine particles is very arduous and fatiguing; only about a dozen estimations can conveniently be completed in a day.

TABLE  
CORRELATION BETWEEN COUNT AND PHOTOMETRIC VALUE  
OF DUST FROM MINE DRIFT AFTER BLAST

Photometric Light Value	Dust Count	Ratio Light Value/Count
1500	1536	0.98
830	877	0.96
840	844	1.00
730	788	0.94
450	499	0.90
450	492	0.91
420	448	0.94
390	421	0.93
390	415	0.94
340	394	0.86
330	380	0.87
300	334	0.90
300	329	0.91
250	248	1.00
140	100	1.40
120	88	1.35
80	82	0.98
100	82	1.22
80	75	1.06
Average =		0.99

We have recently developed a method which obviates this difficulty. Instead of counting the particles, the amount of light reflected by the dust spot under the dark field is measured photometrically. Under standard conditions this is proportional to the surface of the dust recovered. The light may be measured either by a comparative photometer or a photo-electric cell. The foregoing Table shows some of the results obtained by this method.

The samples were taken in a drift following blasting while the dust was being removed by a method to be described later. The size of the particle was about the same throughout, and the constancy of the light value to count ratio is noteworthy. This photometric method is also much more rapid and simpler to do; as many as one hundred samples or more may be estimated in a day. It should greatly facilitate a closer check on the actual dust exposure of the

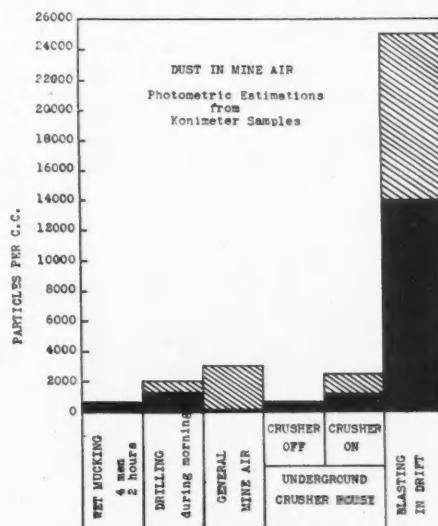


FIG. 1

men in industry. Only by the correlation of such information with clinical findings can the true dangerousness of the dust hazard be estimated. In Fig. 1 are illustrated some representative dust concentrations encountered in mining operations, as measured by this method.

It will be noted that the highest dust concentrations in which the men work are encountered in drilling and blasting operations. Blasting, however, raises much the most dust. Most of the blasting underground is done in either stoping or drifting operations. In stope blasting the men do not go back into the dust until the next shift, but in drifting and crossecutting they return to the face after a blast, passing through

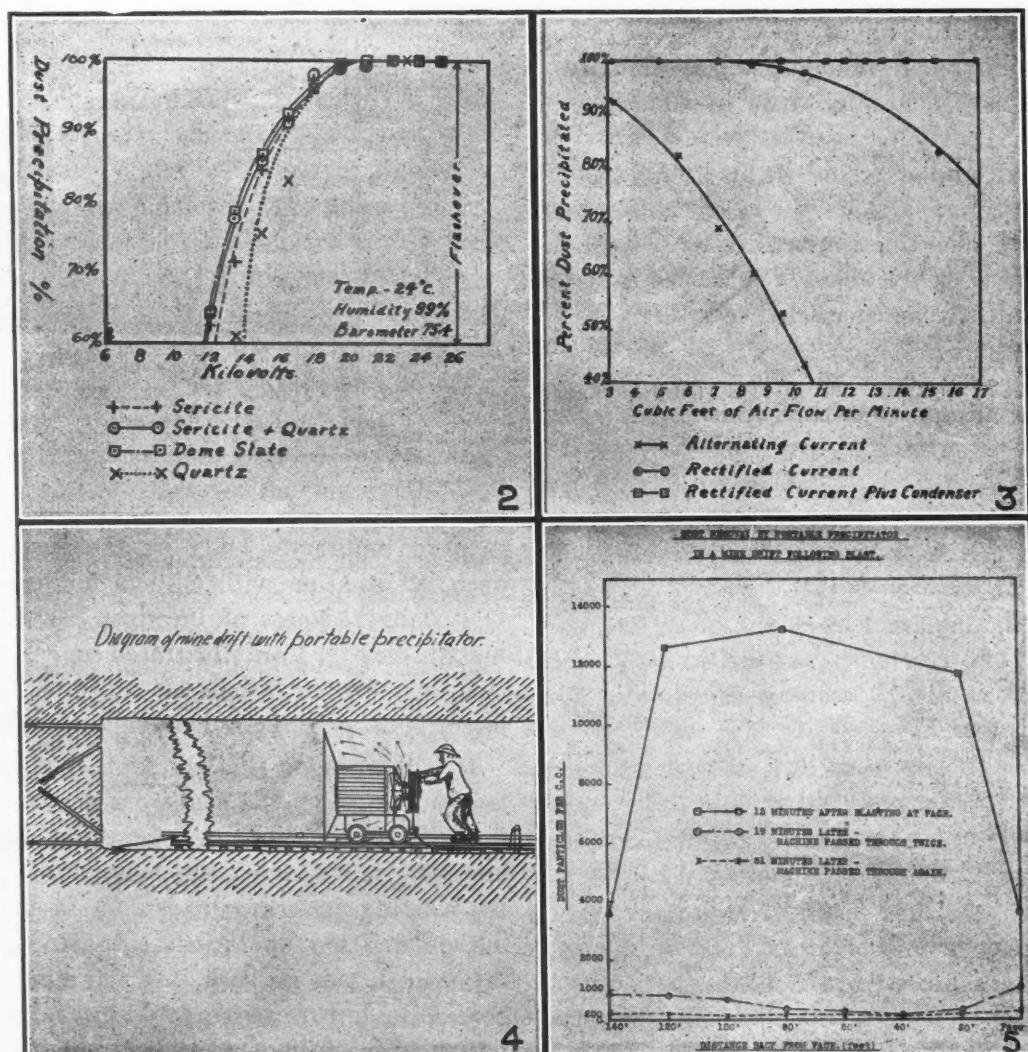
the heavy dust cloud. This dust not only is of the highest concentration but is of the smallest size, and is consequently the most dangerous.

Experiments looking to remove this hazard have been in progress for some time. Any method of successfully removing this dust must fulfil the following requirements. (1) It must remove the fine dust. (2) It must do this rapidly. (3) It must be of such a kind that it can be used where blasting is in progress.

A survey of the methods hitherto used for dust removal showed that electrical precipitation, as originally applied by Lodge, and later developed by Cottrell, would probably fulfil the first two requirements. In this the dust-laden air is drawn through a metal pipe, down the centre of which is suspended a wire on which is placed a high electric charge (to give a corona effect). A stream of electrons thus passes from the wire to the metal pipe which is grounded. As the dust particles are drawn through they pick up a charge and are swept by the electric bombard-

ment to the grounded pipe wall. The effect of such a device on silica dust was consequently studied. Fig. 2 shows that silica dust can be completely precipitated by this method, thus fulfilling the first requirement. The second requirement—rapid precipitation—is seen to be accomplished in Fig. 3. Thus a tube 2 inches in diameter and 15 inches long was found to reduce to safe levels about 8 cu. ft. of air per minute.

A method of meeting the third requirement—ability to be used where blasting operations are in progress—is illustrated diagrammatically in Fig. 4. This was done by mounting a precipitator unit designed to treat 3,000 cu. ft. of air per minute on a mine truck, the whole machine to be pushed ahead of the men as they returned through the dust cloud cleaning up the dust in front of them. The dust-laden air of the drift is brought into the machine by means of a hood. An efficient clean-up is obtained by deflecting the clean exhaust air from the machine into the



irregularities of the drift as it passes along and the dust therein is blown forward and drawn into the machine. The machine is likewise retired with the men during the next blast.

Such a machine has been constructed under the auspices of the Ontario Mining Association. The precipitator unit consists of 200 two inch tubes mounted on mine truck wheels. This is fitted with a suction fan, the power being supplied by a trailing cable. In Fig. 5 is shown the performance of the experimental unit on passing through the dust cloud formed by an explosion in a mine drift. The abscissæ are given as distance in feet back from the face where the explosion occurred. It will be seen that the first requirement is successfully met, in that the dust is reduced to safe levels. Furthermore, the dust from this blast, being removed at its source, is prevented from contaminating the general mine air. The time required (30 minutes) is, however, rather long. Most of this is due to the difficulty of getting all the dust from the irregularities of the drift into the machine. The third requirement—use under blasting conditions—is met, except that on some occasions the rock thrown out on the track makes it difficult to advance the machine near to the face. A further problem was found in the nitric oxides and ozone formed by the corona in the machine. Experiments on animals exposed to the exhaust of such a corona showed no toxicity after 6 months' daily exposure for

two hours. But due to the necessity of a well-marked cyclonic action to reach all the dust considerable recirculation takes place, with resultant accumulation of gas. However, war experience has shown that gas removal offers no insurmountable problem and is simple as compared with the removal of particulate matter. It is thought that with the cooperation of the mine operators, development along these lines should make much of silicosis preventable by removing the inhaled cause.

In the building of the dust precipitator, we have to acknowledge the technical assistance of Mr. F. L. Harrison and others of the staff of the Ontario Hydro-Electric Power Commission Laboratories. The work in the field has been done with the cooperation of Mr. R. J. Ennis and Mr. A. D. Campbell, of the McIntyre Porcupine Mines. The dust estimations have been carried out with the assistance of Miss L. Tresidder, and the tissue culture work with that of Miss A. J. Watt.

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TUBERCLE BACILLI IN THE CIRCULATING BLOOD.—W. Kolle and E. Küster report investigations which altogether fail to confirm the claims made by E. Loewenstein, who has found tubercle bacilli circulating in the blood of some 50 per cent of the subjects of tuberculosis, and in considerable proportion of cases of rheumatic polyarthritis, schizophrenia, and multiple sclerosis. Following Loewenstein's technique, the authors have made 1,033 examinations of 953 patients suffering from tuberculosis or from one of the other diseases already referred to. Positive results were obtained in only 7 cases. In one of these 7 cases the bacilli were found by animal experiments to be virulent. In 5 of the 7 positive cases the disease from which the patients were suffering was tuberculosis, definite or suspect. Among the 111 rheumatic cases, which included some of erythema nodosum, there was only one positive blood finding. The remaining positive finding belonged to the group of 128 cases of schizophrenia and allied conditions. All the 15 cases of multiple sclerosis and all the 68 cases of various other diseases yielded blood in which no tubercle bacilli could be found.—*Deut. med. Wchnschr.*, 1934, p. 309.

According to Flinn and Inouye, only a small fraction of ingested copper is eliminated promptly in the urine. Therefore the study of the latter excretion in man is not without interest at this time. At the Montreal General Hospital, Rabinowitch has carefully examined the urine of fifty persons selected at random except that histories were carefully taken in order to exclude cases in which there was any suggestion of undue exposure to copper through treatment or occupation. From the analytic results, copper appears to be a constant constituent of urine of normal persons. The amounts found ranged between minute traces and 0.4 mg. per litre and between traces and 0.7 mg. for twenty-four hours. In two copper "balance" experiments in which the subjects were fed copper, the amounts were appreciably larger. Obviously, people consume quite unwittingly, day by day, far larger quantities of copper than the data presented indicate. Probably there is more actual danger at present of excessive intake than of deficiency in the human dietary. At any rate the hasty inclusion of copper in present-day therapeutic programs may be ill-advised. Intensive study of the problem for man is imperative.—*J. Am. M. Ass.*, 1933, **101**: 212.

## CYSTINURIA AND CYSTINE LITHIASIS\*

BY FRANK S. PATCH, B.A., M.D., F.R.C.S.(C.),

*Montreal*

**C**YSTINURIA and cystine lithiasis are generally regarded as comparative rarities. And yet cystinuria is the most common of all the so-called "inborn errors of metabolism", and in all probability would be more frequently recognized were those doing routine urinalyses more familiar with the characteristic crystals of cystine, and constantly on the watch for them in urinary sediments. Similarly, cystine calculi would be diagnosed more frequently were all calculi subjected to chemical analysis.

The occurrence recently of a case showing this condition, and its tardy recognition in a brother of the patient who had been operated upon for calculous pyonephrosis ten years previously, together with the many interesting problems connected with the subject, seem to warrant a report of the two cases and a brief discussion of the subject.

## CASE 1

William C., aged four, was admitted to the surgical service of the Montreal General Hospital, September 8, 1921, for rectal prolapse. The parents had noticed a protrusion of bowel at stool two months previously. This had recurred frequently. The boy was also reported to have had difficulty in urinating. He was brought to the Outdoor Department on August 24, 1921. A note was then made of urinary frequency; "the child pulls at the penis"; "urination is painful". On August 31st, he was catheterized for urinary retention, and again, on September 1st. On September 2nd, the catheter was blocked in the membranous urethra, but it passed the obstruction and the urine was removed. An x-ray, September 3rd, showed a shadow, "fairly large, dense and circular, in the midline below the pubic arch". This was regarded as a urethral calculus. A large group of shadows was noted in the left kidney region. That same evening retention recurred. The catheter was blocked, and at the point of block a grating was felt. Under an anaesthetic a stone was palpated about the penoscrotal junction. After attempts to remove it by forceps failed it was removed by external urethrotomy. No note was made of the character or composition of the stone. The wound healed well, but fever developed and pyuria was noted. Cystoscopy was performed on September 27, 1921, with a 18 French cystoscope under ether anaesthesia. The bladder was normal. The common specimen contained much pus, as did the left ureteral specimen. The right ureteral specimen was normal. Urea: right, 0.9 per cent; left, 0.4 per cent. The left kidney was removed, September

20, 1921. The kidney was large. The stone was firmly wedged in the pelvis. Pyelo-lithotomy was discussed, but on account of the infected condition of the kidney a nephrectomy was done. Recovery was uneventful.

Pathologist's report.—(S. 21. 812. Dr. L. J. Rhea). "Kidney weighs 75 grm. and measures 8 by 6 by 3.5 cm. There is a small amount of perinephritic tissue attached. Capsule is smooth and glistening. On palpation several hard, somewhat movable masses are felt. The pelvis incised contains 4 calculi, yellowish green, of irregular shape with faceted surfaces. The cortex measures 6 mm.; its markings are distinct. The surface is greyish-pink in colour. The calyces are uniformly moderately dilated. The pelvis is smooth and glistening. No pus apparent. No tuberculosis. Capsule strips easily, exposing a smooth surface studded with petechial haemorrhages. It is pinkish-grey for the greater part, the remainder being irregular areas of greyish-white covering about one-half of total surface. On section there are similar areas of greyish-white extending to the pelvis."

"*Diagnosis.*—Nephrolithiasis with diffuse chronic inflammation of kidney. Calculi are composed of uric acid."

This statement as to the composition of the calculi has given rise to considerable conjecture, when, as will later be shown, the boy was found to be a cystinuric. Neither the kidney nor the calculi in it have been preserved. In all probability the diagnosis was made by observation only, for it was not until several years afterwards that facilities were available for routine chemical analysis of calculi. It is well known also that uric acid and other calculi very closely resemble those composed of cystine. Moreover, cystine calculi are frequently found mixed with other urinary constituents. In view of the subsequent developments, it is quite possible, indeed very probable, that the calculi were composed of cystine. This lad, who is now 17, has been apparently quite well since the operation 13 years ago. Since his cystinuria was discovered in 1932, his urine has been repeatedly found to contain cystine crystals, the last examination being made on May 29, 1932.

## CASE 2

John C., aged 17, brother of the preceding was admitted to the surgical service of the Montreal General Hospital, on October 24, 1931, suffering with right-sided abdominal pain and vomiting. A diagnosis of acute appendicitis was made, but a normal appendix was removed. There had been no complaints associated with the urinary tract, though the pain was reported as being colicky. After the operation, an x-ray was taken, which showed a large shadow

\* From the Departments of Urology and Metabolism, the Montreal General Hospital, Montreal.

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in the left renal area. He was, thereupon, transferred to the urological service. A cystoscopy was done on October 31, 1931. This confirmed the presence of a stone in the left kidney. There were evidences of trauma about the right ureteral orifice, suggesting the passage of a calculus. A left nephrolithotomy was performed on November 13th and two large stones were removed. Recovery was uneventful. Metabolic studies showed a reduction of renal function. Blood urea nitrogen, 24 mgm. per 100 c.c. Urea concentration factor, 24. He was discharged from the hospital on December 4, 1931.

He was readmitted on May 3, 1932, with a left renal colic of a few hours' duration. The urine contained red blood cells. There was a frequent desire to void. The patient was chilly and had vomited. X-ray showed a number of small shadows in the left kidney. Cystoscopy and pyelography demonstrated that they were renal calculi. No action was taken at this time, and he was discharged from hospital. He was readmitted on October 6, 1932. In the interval he had been free from symptoms until the day previous, when he was seized with a severe colicky pain in the left loin, radiating to the groin. X-ray examination was as on previous admission, except that a small shadow was noted in the upper pole of the right kidney. Urinalysis showed a trace of albumin, and urates. Cystoscopic examination was negative. Pyelography showed the kidneys to be normal, except for slight blunting of the calyces of the left kidney. The shadows were intra-renal. The urines from both ureters contained a few pus cells, but no bacterial growth was found on culture. October 12th, the stones, seven in number, were removed from the left kidney by nephrolithotomy. The pelvis was intra-renal and the kidney very adherent to the surrounding fatty capsule, making operation rather difficult. The day following operation characteristic cystine crystals were noted in the urine by an observant intern. This revelation prompted an immediate chemical examination of the stones. They were found to be composed of 90 per cent pure cystine. One of the laboratory technicians pointed out that there was a similar stone in a bottle, in which it had been for a year or so. This was examined and found to be pure cystine. It was discovered that this was the calculus removed from the same patient one year previously. Its unusual character had evidently aroused curiosity, and it had been sent to the laboratory for chemical examination. The fact that it was not reported upon had been overlooked and the incident forgotten.

The boy's wound healed normally. His urine was found on repeated occasions to contain cystine crystals. He was retained in hospital until December 10, 1932, mainly for the purpose of making complete metabolic studies, details of which will be given later. The members of the boy's immediate family were examined for the presence of cystinuria. The father, mother, one brother and two sisters were negative, but one brother (Wm.C., Case 1) was positive; cystine crystals were isolated in pure form, and chemical identification made. This was the lad whose left kidney had been removed in 1921 for calculous pyonephrosis.

In spite of the treatment instituted there has been a recurrence of calculus in the left kidney, with progressive increase in the size and number of the calculi. That in the right kidney has also continued to increase in size. The last x-ray taken, May 25, 1934, is shown in Fig. 5. Cystine crystals were noted continuously, the last examination being made on May 29, 1934.

**Historical.**—Cystine was first discovered by Wollaston in 1810, in two specimens of bladder calculus. It was styled by him "cystine oxide". Later, at the suggestion of Berzelius (1833) the

name was changed to "cystine". Since this time, an increasing amount of literature, clinical, and, more recently, on the biochemical aspect of this problem, has appeared. In 1916, Kretschmer collected 107 cases of cystine lithiasis. It is very probable that the actual number of cases observed is much larger, owing to the failure of individuals to report their observations.

**Chemistry.**—Cystine is a normal constituent of protein and is obtained in greatest amounts from keratin-containing tissues (horn, hoof, feathers, hair, etc.). It is an amino-acid and is the principal, if not the only, sulphur-containing body which results from the hydrolysis of simple protein. Nutritional experiments have clearly shown that cystine is a necessary component of the diet, in order to maintain health and growth. During its destruction by the body the nitrogenous part is largely converted into urea, and the sulphur portion is largely oxidized and excreted in the urine as inorganic sulphate. Another pathway is through taurine, a normal constituent of bile. Cystine is almost insoluble in water, alcohol, and ether, but it dissolves readily in dilute mineral acid, ammonia and solutions of caustic alkalies, and the alkaline carbonates. It is insoluble in acetic acid. It crystallizes from its solution in ammonia in typical hexagonal, colourless, highly refractile plates or prisms when the solution is allowed to evaporate (see Figs. 1 and 2). Crystals for microscopic examination are conveniently obtained in this manner on a microscope slide. The sulphur in cystine is held in loose combination and is partially evolved as hydrogen sulphide on boiling with alkali. This helps to distinguish it from other amino-acids, and also explains the odour of hydrogen sulphide which results when urine containing cystine is allowed to decompose. If cystine is heated on a platinum foil it burns with a bluish-green flame without melting. The amounts found in urine are never very great. Even in cystinurics, the amounts are small, but cases have been reported with excretions of one-half to one gram per diem. There are a number of methods of identifying cystinuria, but the isolation of the cystine crystals in pure form is the most reliable. The relative merits of the more common reactions used clinically will be dealt with elsewhere.

**Metabolism.**—In cystinuria, due to what Garrod calls "an inborn error of metabolism", the liver allows an excess quantity of cystine to escape conversion into urea. It has been sug-

gested that cystinuria is due to incomplete oxidation of the cystine unit with protein. This is based upon the finding at times of putrescine and cadaverine and, more rarely, leucine and tyrosine. It is doubtful, however, whether the presence of cystinuria is due to inability of the body to metabolize cystine, since cystinurics are able to metabolize large quantities of ingested cystine. Dr. Rabinowitch is of the opinion that we are dealing with a condition analogous to the glycosuria in renal glycosuria. In this condition glucose appears in the urine as a result of an undue permeability of the kidneys to sugar, and not from any failure of the patient to oxidize glucose; the blood sugar is normal in this condition. In cystinuria, there is probably a lowered liver threshold for cystine in the blood. There thus appears to be no relationship between blood concentration and urinary excretion.

Cystinuria is a comparatively rare condition. According to various authors, it is found in from 1 in 15,000 to 1 in 35,000 persons. This is based on the findings of the crystals in the urine. Newer laboratory methods suggested by Brand and Sullivan have shown the presence of cystinuria where the crystals have not been found. Using the Brand and Sullivan tests, Lewis has demonstrated 29 positive cases in 11,000 healthy young individuals (1 in 320), a much higher percentage than was previously thought the case. It must be borne in mind, however, in the interpretation of the Brand and Sullivan tests that the colour reaction is not specific for cystine. It is given by any compounds which contain the free S-H group. It is doubtful, however, whether, apart from ergothioneine and glutathione, there are other compounds in appreciable quantities in the human body which contain the S-H group. The reaction of Brand and Sullivan, though not specific for cystine, is much simpler and probably more sensitive than the chemical isolation of cystine crystals. The relative sensitivity might, therefore, explain the high incidence of cystinuria noted with this reaction.

As cystinuria is symptomless it is often overlooked, and even where cystine calculi are present their true nature is not suspected, as in our first case. When it does appear, it does so in early life, rarely after 50. The hereditary tendency and the strong familial character are very marked. In our series it occurred in two

brothers. Kretschmer reported cystinuria and cystine lithiasis in twin brothers. Robson observed 12 cases in three generations, in whom several deaths apparently directly or indirectly attributable to the derangement had occurred. Graves found 8 cystinuric members in two generations in the family of the patient whom he treated for cystine stone. The most remark-

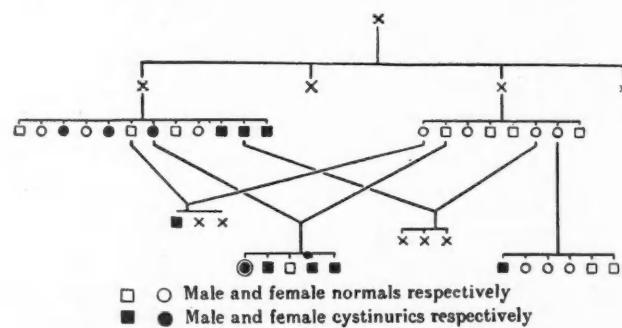


CHART 1.—Showing familial character (Robson).

able occurrence in this respect concerns the progeny of two half-brothers, reported by Thin. The older had 12 children; 5 of these had cystine lithiasis; 2 were cystinurics. Of his grandchildren, 2 had lithiasis, 4 had cystinuria. The younger half-brother had 10 children, none of whom had cystinuria. Three of his children married their cousins, children of his older half-brother. Their children in 2 cases were afflicted with cystinuria. One of his daughters married a distant relative and had one son who had to have an impacted calculus removed from a ureter.

*Lithiasis.*—The percentage relation of cystine calculi to all other calculi varies largely, according to different authors. Pousson and Carles state that they occur in a percentage of 0.26. Lamy gives a percentage of 0.57, while Nakano gives as high a percentage as 1.16 and Kuster 2.5. According to Gottstein, it is generally thought that 2.5 per cent of cystinurics develop cystine lithiasis.

A cystinuric afflicted with lithiasis does not necessarily form cystine calculus, and, at times, the cystine is found mixed with other salts. It is a mistake to think that cystine calculi are always unilateral; they are frequently bilateral. Most authors admit a strong tendency to recurrence. Garrod suggests that infection of the urinary tract may play an important part in the formation of this type of calculus, as of those of other materials. He points out that a cystinuric with sterile urine may live for many years without forming calculi, and

suggests the use of measures directed against urinary infection in such cases. And yet there are cases reported of cystinurics with sterile urines, who formed stones persistently, and others with markedly infected urines who did not form calculi.

Cystine calculi are of a light amber or fawn colour, and are somewhat waxy in appearance.

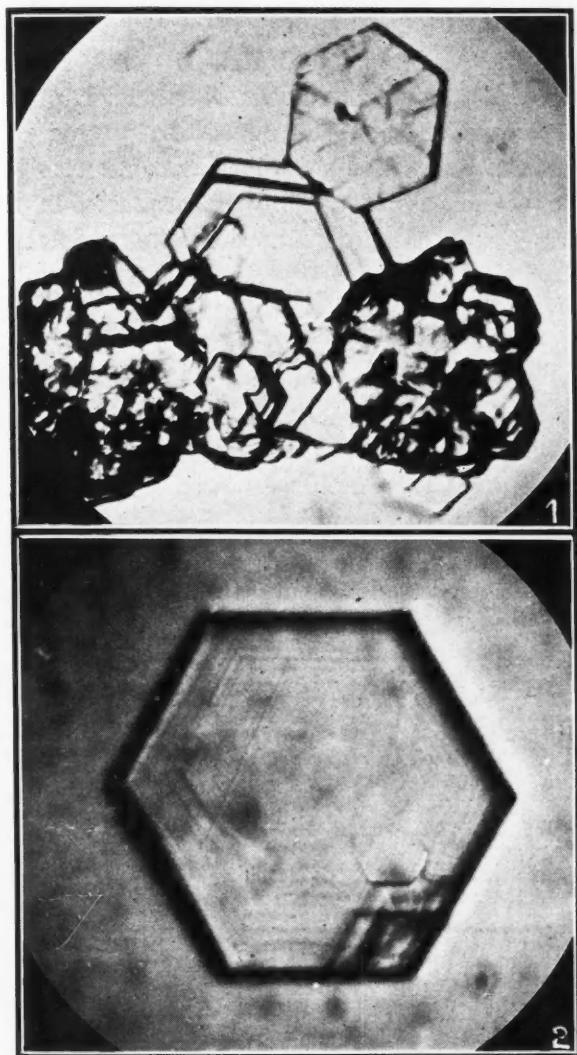


FIG. 1.—Cystine crystals isolated from the calculus in Case 2, with clear demonstration of a single crystal.

FIG. 2.—Enlargement of a single crystal.

They are granular and glistening. According to some they are rather soft and friable. On section they show a pale green and waxy appearance. It is stated that after exposure to light, the green coloration is accentuated. They may be readily confused with uric acid calculi, unless a careful chemical examination is made. Braasch points out that, as cystine calculi are frequently unilateral, there may be an anatomical factor in the kidney itself to account for

the formation of calculi. In neither of our cases was any factor found, other than that resulting from the presence of the calculi, in producing dilatation and infection of the kidney.

In our opinion, there is no essential difference between the lithiasis produced from cystine and that of other materials, with the one exception that in cystine lithiasis a definite disorder of metabolism is associated. It may be remarked that in calculus formation generally an error of metabolism may equally well be present. Recent experiments with diets deficient in certain vitamins strongly favour this assumption. Certainly, the factors which favour the formation of urinary calculus in general will favour the production of cystine calculus. The same effects of obstruction, dilatation and infection, may follow. From the point of view of symptomatology, diagnosis, and treatment, there is but little difference, and these matters, with a few undermentioned exceptions, call for no special consideration in this paper.

With regard to the visibility of cystine calculi, there seems to be a general impression that cystine calculi cast a faint shadow in an x-ray picture. According to some, xanthine and cystine give the faintest shadows of all calculi. This is said to be the case particularly with pure cystine calculi. In Graves' case there was no demonstration of the calculus in repeated x-ray pictures. On the other hand, Holmes and Ruggles state that phosphates and cystine are the densest of all calculi. Other authors agree with the view that cystine calculi are quite opaque. Our own experience in the two cases conforms to this opinion, and in our second case the calculi were almost pure cystine. It may be that the small stones are not readily seen, as some infer. In any event, in view of the contrary findings, as in Graves' case, one should take special precautions in patients who give a negative x-ray and have cystinuria or a positive result to the tests of Brand and Sullivan. In such cases, further methods of investigation should be used, including that of the wax-tipped catheter.

With regard to medical treatment, many efforts have been made by dietary control and alteration of the reaction of the urine to prevent calculus formation, or, once resulting, to bring about its dissolution. Most authors stress the importance of a low protein diet. It may be pointed out, however, that a cystinuric is able

to metabolize cystine readily, even when it is given in large quantities. Largely because of the ready solubility of cystine in a dilute alkali, efforts have been made to bring about a dissolution of the offending calculus by the internal administration of alkalies. Kretschmer states that Cantani and Klemperer and Jacoby recorded "remarkable results" with this method. Beale claims successful results in a patient he had observed during a period of fifteen years. The patient, a cystinuric, had passed "hundreds of small calculi" and had had a bladder stone crushed by lithotripsy. Following the administration of ammonium carbonate, 50 grains per diem, over a period of a year, the calculi decreased in number, and in the last three or four years none had been passed; the cystine crystals were still noted in the urine but in smaller amount. Crowell and Reaves claim to have produced dissolution of large calculi in the kidney pelvis by the use of sodium bicarbonate, and pelvic lavage with an "alkaline antiseptic solution". Reaves' case had an associated *B. coli* infection. The subsidence of infection and complete disappearance of the calculus in the kidney occurred in a period of three weeks. The patient had taken 60 grains of the sodium bicarbonate daily during this period. In both of these cases, the cystine crystals disappeared from the urine. It is not surprising that some authors even question the wisdom of surgical interference, in view of the extreme tendency to recurrence after the operation.

The unsuccessful result of surgery in our

second case, prompted us to make similar therapeutic experiments. With the active cooperation of Dr. I. M. Rabinowitch, Director of the Department of Metabolism, the patient was subjected to a course of treatment under careful observation.

First of all, cystine obtained in pure form from the patient's calculi was exposed to solutions of pH ranging between 5.8 to 8.2. These were kept in an incubator at 40° C. from November 18, 1932, to March 11, 1933, that is, for a period of 113 days. No solution of the cystine was observed, in spite of a pH as high as 8.2, a degree which is incompatible with life and which cannot possibly be produced in the body by the administration of alkali. The patient himself was maintained from November 3 to 9, 1932, on a weighed diet. During this time the CO<sub>2</sub> combining power of the plasma and the pH of the urine were determined periodically. The patient was then given an "alkaline ash" diet. There followed no alteration in the CO<sub>2</sub> combining power of the plasma, nor in the pH of the urine.

Following his discharge from the hospital, December 10, 1932, he was asked to follow an alkaline-ash-low protein diet, consisting of approximately 352 grm. of carbonydrate, 70 grm. of fat, and 50 grm. of protein daily. He was instructed to take 160 grains of sodium bicarbonate daily. This was done until January 5, 1933, according to the patient, faithfully. The patient was instructed how to test the reaction of the fasting urine with litmus. The urine was

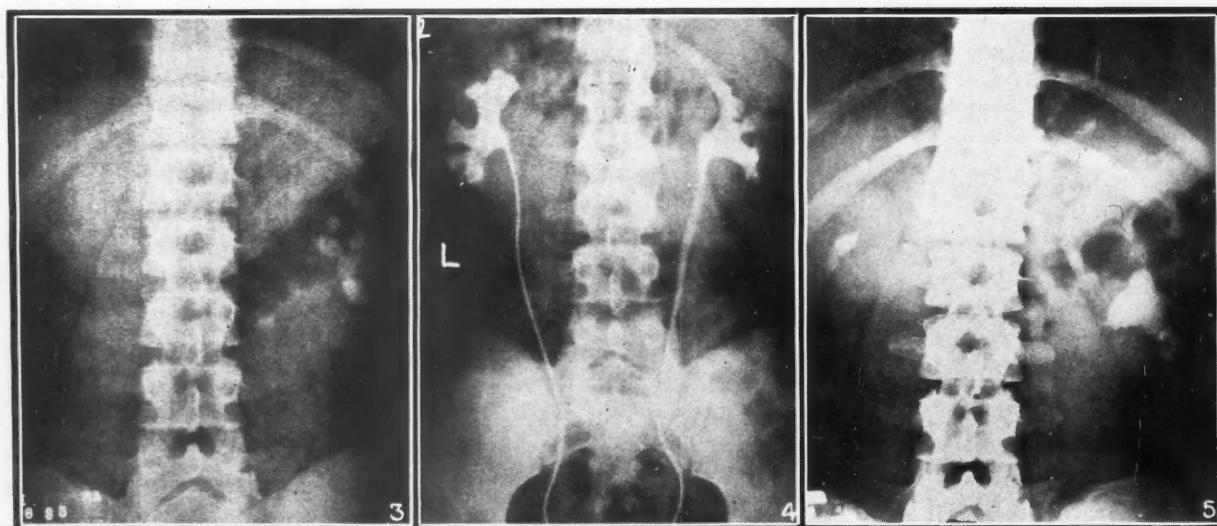


FIG. 3. Case 2.—X-ray; first recurrence of calculus, October 7, 1932.

FIG. 4. Case 2.—Pyelogram, October 7, 1932.

FIG. 5. Case 2.—X-ray; second recurrence of calculus, May 25, 1934.

continuously alkaline and was tested daily. On January 5th, the dose of sodium bicarbonate was increased to 200 grains per dram. On June 2, 1933, the urine was alkaline, with a pH of 7.7.

X-ray examinations have been made from time to time. There has not been the slightest improvement. On the other hand, there has been, in both kidneys, particularly in the left, a progressive increase in the size and number of the caleuli. Infection has, fortunately, been absent, or, at the most, minimal. His urine on May 29, 1934, showed no pus, the only abnormal constituents being cystine crystals and an occasional red blood cell. He has been free from painful symptoms, and his general health has been excellent. In spite of the successful results obtained by some authors with alkalinization of the urine, we have to admit a complete failure in our efforts not only to prevent recurrence of the caleulous lithiasis but, also, extension of their growth. This is in accord with the experience of many others.

It should be pointed out that, in many instances, surgical intervention has been followed by perfectly satisfactory results, without recurrence, even where no dietary control has been maintained and no efforts have been used to alter the reaction of the urine. Surgery was successful in our first case, in which a nephrectomy was performed. In spite of a cystinuria, presumably persistent, there has been no recurrence of the calculus in the other kidney. Surgical intervention is still possible and is being considered in the second patient who still suffers from bilateral lithiasis.

#### CONCLUSIONS

1. The subject of cystinuria is still veiled in obscurity and no entirely satisfactory explanation has yet been given for its occurrence.

2. In cases of cystinuria most authorities advocate that the patient be placed on a lowered protein intake and given alkalies. Many, however, admit the failure of these procedures, and

claim that no treatment is necessary unless calculi have been formed. Such a patient should, however, be kept under careful observation. Any abnormal factors in the urinary tract or infective foci in the body which would predispose to urinary infection or caleulus formation should be given palliation or correction. Urinary infection should be combated by appropriate measures.

3. Cystine calculi are extremely likely to recur. Surgical intervention, conservative or radical, is our main source of reliance. It may, at times, be most unsatisfactory and discouraging, and recurrences may quickly follow. Dietary control and the use of alkalies internally or by pelvic lavage may be given a trial.

4. Many cases of cystinuria are not recognized. More careful urinalysis is advised in order that cystine crystals may be detected in the urinary sediment. The tests of Brand and Sullivan should be more generally used.

5. The presence of cystine in caleuli is frequently unrecognized. All calculi should be subjected to a careful chemical analysis.

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Philosophy, thou guide of life! Thou searcher after virtue and banisher of vice! What would not only we ourselves but the whole life of men have been without thy aid! It is thou that foundest cities, gatheredst men in social union; thou that united them together first in dwellings, then in the nuptial tie, then in the pleasures

of literature and the interchange of speech: to thee we owe the devising of laws, and thou didst guide men to righteous ways and virtuous habits. To thee we come for refuge; from thee we seek for help. One day well spent according to thy precepts is preferable to an immortality of sin.—Cicero.

## XANTHOMATOSIS AND THE SCHÜLLER-CHRISTIAN SYNDROME: A ROENTGENOLOGICAL AND CLINICAL STUDY\*

BY SAMUEL REICH, M.D.,

Vienna

**XANTHOMATOSIS** is of special interest to the roentgenologist because both its diagnosis and treatment lie in his hands. Inasmuch as only 55 cases of this disease are recorded in the literature the description of every new case, with its peculiarities, is of value in adding to our knowledge.

### CASE REPORT

A boy, aged four years, was sent from the Department of Paediatrics of the Royal Victoria Hospital for examination of his skeleton, with the report—"Peculiar posture and bad gait."

**X-ray findings.**—"Multiple cystic rarefactions in each os ilium, in each os pubis, in the epiphysis (head) of the left femur, in the shaft of each femur, in the epiphysis of the head of the left humerus, and in the shaft of the right humerus. The defects of the bones are sharp but irregularly limited. They are centrally located, extending to the cortex, but not penetrating it. The periosteum shows no reaction. The picture resembles osteitis fibrocystica-Recklinghausen. (See Figs. 1 and 2). The picture of the skull shows many irregular map-like defects in the vault. The defects of the bones have the appearance of operative defects. (See Fig. 3). The sella is eroded. There are no changes in the bones of the jaw."

\* From the X-ray Department of the Royal Victoria Hospital, Montreal, Dr. A. H. Pirie, Director.

These findings caused Dr. Pirie to suggest the diagnosis of xanthomatosis. The clinical features and the comparison with the literature confirmed his opinion.

**Personal history.**—The child's birth was normal; development until two years of age, normal; no children's diseases. For the last two years he had developed poorly, had lost his appetite, and did not play with other children. A discharge from both ears and diabetes insipidus developed.

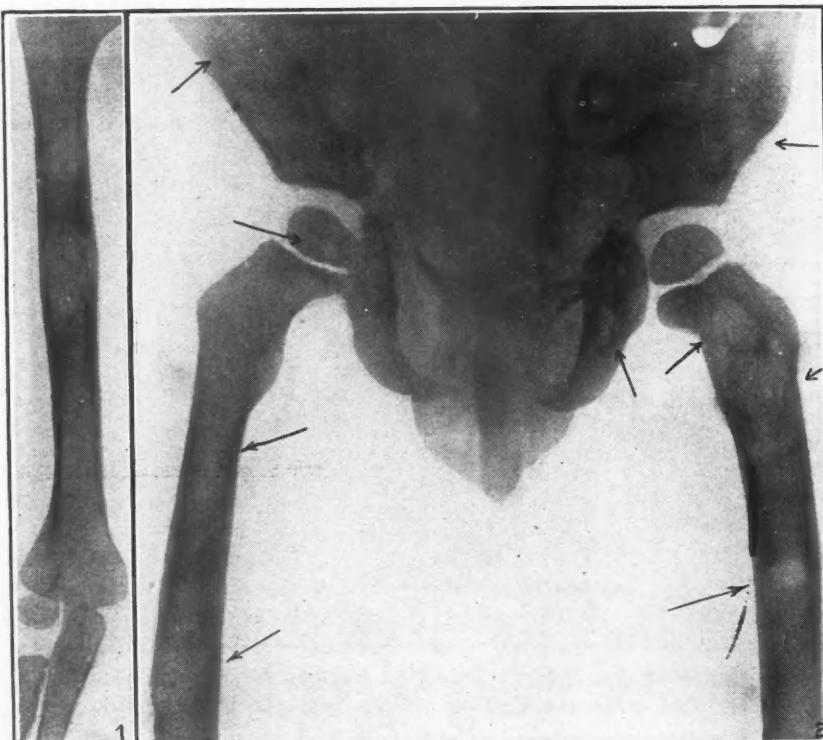
**Physical examination.**—The patient showed a peculiar posture and a bad gait. He kept his vertebrae stiff and limped slightly, but both extremities were equal. The bones did not show any pathological changes and were not tender. In the skin of the nose, face, extremities, and trunk were multiple small yellow-brown nodules, probably xanthoma tuberosum. The head of the patient was slightly larger than normal; the fontanelles were closed. There was no craniotabes; no exophthalmos. Discharge from both ears, and decay of the teeth and soft gums were noted. There was slight enlargement of the lymph glands. The lungs and heart were normal; the spleen and liver, not enlarged. The bones did not show anything pathological. The Wassermann test was negative. There was no reaction to 1 mg. of tuberculin. Urine normal. The Bence-Jones albumose test was negative. The blood showed slight hypochromic anaemia, otherwise negative; haemoglobin, 70 per cent; erythrocytes, 3,800,000. The cholesterol in the blood was 140 mg. per cent (normal).

**Summary.**—The patient showed defects of the membranous bones, defects in the long bones, diabetes insipidus, and xanthoma tuberosum of the skin. One main symptom of the Schüller-Christian syndrome, exophthalmos, was absent. In addition, otitis and stomatitis, with a general enlargement of the lymph glands, were present, which symptoms frequently occur in xanthomatosis.

### REVIEW OF THE FIRST CASES OF CHRISTIAN, SCHÜLLER AND HAND

The first case was reported by Hand<sup>1</sup> in the year 1893 under the title "Polyuria and Tuberculosis".

The patient, a boy three years old, showed diabetes insipidus, exophthalmos, a papular eruption of the skin, bronzed skin, enlarged spleen and liver. He died from bronchopneumonia. The autopsy disclosed yellow nodules in the skull and liver.



Hand examined these and diagnosed tuberculosis, but he was not satisfied with his own diagnosis. He considered the disease to be a tuberculous granuloma of the bones which caused dyspituitarism by its localization near the hypophysis. He was therefore nearer to the reality than Schüller and Christian by whom the disease was named.

The first x-ray pictures showing the typical map-like defects of the skull were taken by Schüller<sup>2</sup> in Vienna.

His first patient was a boy, 16 years of age, with dystrophia adiposo-genitalis, diabetes insipidus, exophthalmos, and discharge from the right ear for the previous four years. The x-ray picture showed typical defects of the membranous bones of the skull.

Schüller assumed a tumour or angioma of the base of the skull near the sella to be the cause of the syndrome.

His second patient was a girl, 4 years of age, with exophthalmos, diabetes insipidus, and roentgenological defects of the membranous bones of the skull.

He now diagnosed an anomaly of the skeleton resulting from dyspituitarism. He reversed the causality, considering as primary the dyspituitarism, which caused the decalcification of the bones.

Christian<sup>3</sup> joined in this wrong opinion. He reported in the Osler Memorial Volume, 1919, a case under the title "Defects in membranous bones, exophthalmos and diabetes insipidus: an unusual syndrome of dyspituitarism: a clinical study".

His patient, a girl, 5 years of age, presented loose teeth, diabetes insipidus, exophthalmos of the right eye, and roentgenological defects of the membranous bones of the skull. The sella was also involved.

Christian summarizes all the previous reported cases and defines the disease by the syndrome, defects of the membranous bones, diabetes insipidus and exophthalmos, caused by the disturbance of the internal secretion of the hypophysis. The dyspituitarism is in his opinion primary. Shortly afterwards Hand<sup>4</sup> published another case and criticized in his article Christian's opinion under the title "Defects of

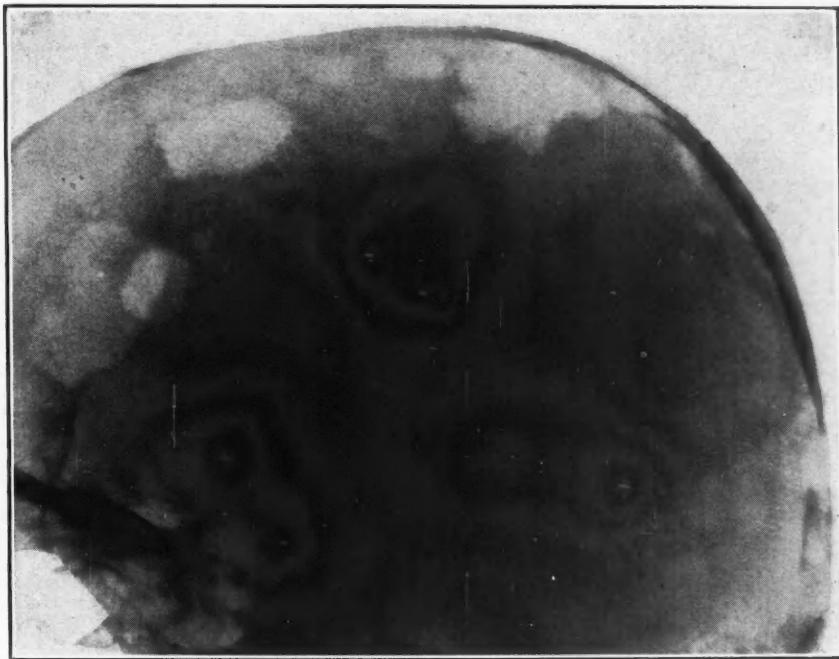


FIG. 3

membranous bones, exophthalmos, and polyuria in childhood—Is it dyspituitarism?"

His patient, a boy, 7 years of age, showed exophthalmos, more marked on the left side than on the right, and pronounced defects of the membranous bones of the skull, but the sella was not involved and the patient did not show diabetes insipidus.

Hand pointed out that the change in the bone affects the hypophysis and causes diabetes insipidus, and that it is not the dyspituitarism that causes the change in the bones. In his own case the hypophysis was not affected, and therefore there was no diabetes insipidus.

#### ANATOMICAL AND HISTOLOGICAL CONSIDERATIONS

The following two cases are important for their anatomical findings.

The patient of Griffith,<sup>5</sup> and of Weidman and Freedman,<sup>6</sup> (Case 2), a boy of 9 years, had multiple nodular xanthomas of the skin, jaundice, defects in the skull, diabetes insipidus, and exophthalmos. The autopsy showed yellow nodules, 6 to 20 mm., involving both tables of the skull. The same changes were present at the base of the skull, involving the sinus cavernosus, the ganglion Gasserii, and the carotis. The base of the brain between the chiasm and the corpus mammillare, with the posterior lobe of the hypophysis, was infiltrated. The pineal gland was enlarged and infiltrated. Changes of the same nature were present in the lungs. The parenchyma and pleura showed diffuse fibrosis, with yellow patches and storage of lipoid in the septa between the alveoli, which were thickened and infiltrated by lymphocytes. The hilus of the liver was infiltrated, and both hepatic ducts were compressed, thus causing the jaundice.

Microscopic examination showed inflammatory fibrous tissue with much lipoid. The authors thought it was secondary storage of lipoid in syphilitic foci.

A similar case was described by Thompson, Keegan and Dunn.<sup>7</sup> They proved that the exophthalmos was caused by infiltration of the orbits.

Infiltrations were found in the skull, in the petrous part of the mastoid, in the mandibles, and in the sphenoidal and ethmoidal sinuses. The sella was free, but the posterior lobe of the hypophysis, the infundibulum, and tuber cinereum were infiltrated, causing diabetes insipidus. There were defects in the scapulae, clavicles, humerus, ribs, lumbar and cervical vertebrae. The lung showed fibrosis and infiltration with mononuclear and polymorphonuclear cells in the septa between the alveoli.

*Microscopic examination.*—Inflammatory connective tissue with lipoid cells ("foam cells") partly becoming giant cells, plasma cells, lymphocytes, polymorphonuclear and eosinophile cells.

Rowland<sup>8</sup> was the first to suggest, in the case of Weidman and Freeman with the xanthoma of the skin, that the changes in the bones may be of the same nature as those in the skin, and to assert that the Schüller-Christian disease is a xanthomatosis of the bones. He could then prove by an autopsy in one of his own cases that the lesions in the bones and lungs consist mainly of xanthoma cells. The name of "xanthomatosis" for the disease was also suggested by him.

The xanthoma cell is a cell of reticuloendothelial origin, with many lipoid drops in its protoplasm. In fixing the fat is dissolved away and the cell gets a foamy structure; therefore it is also called "foam cell" (Schaumzelle). Accumulations of such cells occur frequently in the skin, being a harmless anomaly. They form little yellow plaques or nodules (xanthoma planum; xanthoma tuberosum). Most frequent is a single plaque in the eyelid, called xanthelasma. The xanthoma also occurs as an eruption in diabetes and jaundice. Further, it has been met with as xanthoma of the tendon sheath, which sometimes extends to the bone. Xanthoma cells in the internal organs, in the mucous membranes, and in the marrow of the bones, without any clinical symptoms, had been reported by different authors previously.

The nature of the disease depends upon the consideration of the xanthoma cells. Virchow considered them to be tumour cells and the xanthoma to be a tumour. In most books on pathological anatomy the xanthoma is described next the lipoma. The lipoma is a simple fat tumour, and the xanthoma is a fat tumour with doubly refractive (anisotropic) fat (lipoid). According to this opinion, xanthomatosis ought to be a tumour-like disease of the bony system.

Many authors, however, doubt that the xanthoma cell is a tumour cell, and consider xanthomatosis to be an inflammation and the xanthoma a granuloma — thus, Bonhomme, Flessig, Weil, Seyler, Marchand, Kitsch, Anders, Spiess, Berti, Wustman, Dunn, Mason and Wollston, Land, Hauptl, Chester. Finally, Anitschkow<sup>9</sup> succeeded in transforming vitally stained reticuloendothelial cells into xanthoma cells by feeding or injecting rabbits with cholesterol. So he refuted the theory as to the tumour nature of the xanthoma cell, because a tumour cell always originates by division (karyokinesis) of an old tumour cell, while the xanthoma grows by the accretion of new cells from outside to the mass. The reaction to the noxious substance we call inflammation. According to this view, xanthoma is a granuloma like the tuberculoma or syphiloma, and xanthomatosis is an inflammation. Chester<sup>10</sup> therefore proposes to change the name "xanthoma" which connotes "tumour", to "lipoid granuloma". He summarizes all the previous histological findings, adding 2 cases of his own, and describes the lipoid granuloma (xanthoma) as follows. "There are three elements in the lipoid granuloma: (1) lipoid cells, which are the specific part of the granuloma; (2) exudate cells which are the reaction of the tissue to the presence of noxious lipoids; (3) connective tissue which acts in healing of the lipoid granuloma."

The lipoid cells are large globular mononuclear cells with foamy protoplasm, in the spaces of which lies the lipoid. There are also polymorphonuclear lipoid giant cells. The lipoid in the cells is partly isotropic and partly anisotropic, and stains with Nile blue sulphate, partly pink, partly violet, and partly blue. The cells are round when they are lying separate, but when in dense masses they lose the cell walls and fuse into a syncytium. At the same time the nuclei begin to disappear. In this way the lipoid cells decrease.

The exudate cells consist of lymphocytes, plasma cells, eosinophiles, and mobile histiocytes. They never contain lipoid.

The connective tissue includes fine fibroblasts and blood capillaries, shrinking fibrous scars, and connective tissue between these extremes, depending upon the age of the lipoid granuloma. Recent forms of the lipoid granuloma consist mainly of lipoid cells; in the later stages the exudate cells prevail and the lipoid cells are

disappearing. Finally, both the lipoid and exudate cells are absent, and the lipoid granuloma consists exclusively of fibrous tissue. Thus, xanthomatosis corresponds exactly with the idea of a specific inflammation like tuberculosis, rhinoscleroma or leprosy, the difference being that it is a non-infectious non-bacterial inflammation. A reticulo-endothelial cell phagocytes drops of lipoid and is transformed into a xanthoma cell, just as a cell of reticulo-endothelial origin phagocytes the lepra or rhinoscleroma bacillus and is transformed into a specific Virchow lepra cell or Mikulicz rhinoscleroma cell. Exudation of cells and fibrotic regeneration complete the picture of inflammation. Thus the lipoid granuloma is a non-bacterial specific inflammation caused by noxious lipoids.

#### X-RAY AND DIFFERENTIAL DIAGNOSIS

The lipoid granuloma attacks by preference the vault of the skull, causing map-like, irregular, but sharply delimited, defects, one of the classic symptoms of the Schüller-Christian triad (map-like skull, diabetes insipidus and exophthalmos). (See Fig. 3). Further, the base of the skull is involved, and frequently the sella is destroyed, which explains the diabetes insipidus; the walls of the orbits are infiltrated and this causes the exophthalmos. The petrous bones, the mastoid, and the jaws show more diffuse, less sharply delimited, areas of decalcification; the bones look as if washed out by the rain. There occur also cystic (sharp) areas of decalcification like those in the long bones. At the roots of the teeth rarefactions and cysts are sometimes found, like an abscess or like epulis. These are the cause of stomatitis, loss of teeth, and deafness, which frequently occur as additional symptoms of xanthomatosis. The bones of the pelvis, ribs, the vertebrae, the scapulae, and the long bones show multiple central cystic rarefactions which extend to the compact bone, thinning it considerably. (See Figs. 1 and 2). Sometimes the cysts are so numerous that the bones have the appearance of a sliced tomato. They are located in the epiphysis as well as the diaphysis. Pathological fractures occur spontaneously, but they heal. The bones do not show any considerable expansion, no bending, no disturbance in growth of the neighbouring parts, and no fibrous decalcified masses such as occur in osteitis fibrocytistica-Recklinghausen or

in enchondroma. An extended sclerosis of the bones may also occur, which makes them structureless, especially in the old forms of xanthomatosis. X-ray pictures of this *in vivo* I have not been able to find. As a matter of fact, the clinicians have not yet observed one case of pronounced sclerosis of the bones in xanthomatosis. On the other hand, Chester examined 12 cadavers with xanthoma of the skin for lipoid granuloma of the bone. Two had xanthomatosis of the bones and both showed sclerosis. Case 1 had pronounced manifestations; Case 2 showed slight sclerosis. Additional cases of sclerosis of the bone and xanthomatosis are reported by Hoefer, Slauck, Donnelly. This proves the sclerosis is not so rare as might be concluded from the fact that it has been rarely observed clinically, but the reason is that the clinician observes recent cases only, with acute symptoms, and considers only Schüller-Christian disease as xanthomatosis; he fails to diagnose the cases without a syndrome. Likewise, the roentgenologist never thinks of lipoid granuloma when finding accidental sclerosis of a long bone without any clinical symptoms. Therefore I wish to point out once more the necessity of thinking of a healed lipoid granuloma when sclerosis of the bone of unknown origin occurs, and of making pictures of the whole skeleton in order that possible defects in other parts of the bones may be disclosed. The fully developed syndrome of the Schüller-Christian disease is easy of diagnosis by every one who knows the symptoms. But forms of xanthomatosis of the long bones which do not involve the skull and do not exhibit the syndrome of Schüller-Christian disease are not extremely rare. So, for example, Kienböck and Schneck,<sup>11</sup> in Vienna, describe a similar case with pathological fracture of the humerus.

An adult patient fell and suffered a fracture of her forearm. An x-ray picture showed a spontaneous fracture in a pathologically changed bone. The whole humerus was full of cysts. X-ray, further, showed the same changes in all the other long bones. In the right forearm the cysts were so numerous that the bone had a tomato-slice appearance. The bones of the skull were free from changes. Diabetes insipidus, exophthalmos, and other clinical symptoms were lacking. The wrong diagnosis, *osteitis fibrocytistica generalisata-Recklinghausen*, was made.

A similar case was described by Kienböck and Moworach.<sup>12</sup> In the sister of Herzenberg's patient defects of the long bones were found without the Christian-Schüller syndrome. Sosman<sup>13</sup> describes a case of lipoid granuloma of the tendon-sheath, with roentgenological de-

fects in the long and small bones of the extremities, without involvement of the skull. Finally, both the autopsy cases of Chester had lipoid granulomas in the long bones and in the vertebræ, but no typical defects in the skull. This proves that these cases are not so rare, but that they are less often observed and later diagnosed than the striking syndrome of Schüller-Christian disease. It is therefore suggested to subordinate the Schüller-Christian disease to the conception of xanthomatosis, instead of coordinating it. We shall call Schüller-Christian disease those cases only which show at least defects in the skull and dyspituitarism; we shall call xanthomatosis (Rowland) all cases of lipoid granulomatous infiltration of the bones, including the Schüller-Christian disease. In this way, Christian will be right in defining his disease as dyspituitarism, and the x-ray man will not be diverted from a correct diagnosis by the identification of xanthomatosis and dyspituitarism.

#### X-RAY AND DIFFERENTIAL DIAGNOSIS

The following conditions have to be considered in regard to differential diagnosis: (1) multiple carcinomatous metastasis, especially the exclusive osteoclastic forms and the cystic shell form; (2) multiple myeloma of the skeleton; (3) the multiple enchondroma; (4) osteitis fibrocytistica generalisata-Recklinghausen.

In carcinomatous metastasis the primary tumour may remain occult, but the typical quick and fatal course of the disease proves the diagnosis. While xanthomatosis runs a protracted course without serious complaints and lasts for decades, it is fatal in 30 per cent of the cases only. A similar consideration applies to multiple myeloma; the complaints here are serious— inability to use the extremities, confinement to bed, anaemia, loss of weight, fever and death. In the x-ray picture, bendings and fractures are more frequently observed than in lipoid granuloma. The Bence-Jones body in the urine is more suggestive of multiple myeloma. In contrast to these two diseases, multiple enchondroma of the skeleton shows a benign course like that of xanthomatosis. On the other hand, the x-ray picture reveals great thickening and expansion of the bone, which does not occur to the same extreme extent in xanthomatosis; also those parts of the bones nearest to the lesions show disturbance in growth.

In osteitis fibrocytistica-Recklinghausen a greater expansion of the bone and more fibrous masses are shown sometimes, but very frequently differential diagnosis is impossible. A biopsy shows, frequently, the typical lipoid granulomatous tissue, but the older forms show no longer the characteristic "foam" cells; particularly is this the case after x-ray treatment, but they show the picture of chronic non-specific inflammation.

Lipoid granuloma of the lung is not rare. Cases are reported by Thompson, Keegan and Dunn,<sup>7</sup> Hochstätter and Veit, Schultz, Wermleter and Puhl, Rowland, Herzenberg, Chester, Sosman, Schüller and Chiari, Kartagener and Fischer.<sup>14</sup> Anatomically, the changes in the lung consist of multiple small, yellow nodules in the pleura and in the parenchyma consisting of specific tissue. There are also fibrous thickenings of the lung septa (see the autopsy report of the case of Schüller and Chiari). Older forms show increase of the fibrous tissue in the pleura pulmonalis, between the lobes and between the alveoli, but in the parenchyma of the lung the connective tissue appears in focal spots only, in small nodules in the centre of which run a small artery and a vein. Xanthoma cells may be absent. These completely fibrous nodules may be regarded as scars following lipoid granuloma. The fibrosis of the lung increases gradually; finally the circulation of the lungs is hindered, causing dilatation of the right heart. Insufficiency of the right heart is the cause of death in xanthomatosis of the lung. (See Rowland's first case). These characteristic anatomical changes in the lungs cause typical changes in the x-ray picture, namely, the appearance of a stippled lung field (*getüpfeltes Lungenfeld*) similar to that of miliary tuberculosis. As xanthomatosis of the lungs may, conceivably, occur without changes in the bones, though a case like this has not yet been observed, the roentgenologist has to consider xanthomatosis in every case of a non-typical stippled lung field without clinical symptoms of miliary tuberculosis. In the matter of differential diagnosis we have to consider the whole chapter of the stippled lung field, namely, (1) miliary tuberculosis; (2) lymphangitis carcinomatosa; (3) bronchiolitis obliterans; (4) the small focus of broncho-pneumonia and scars following it, both in children; (5) pneumonokoniosis; (6) a combination of chronic conges-

tion and emphysema of the lung; (7) Böck's sarcoid, a rare disease, resembling xanthomatosis because it shows a combination of a stippled lung field and changes in the skin.

Xanthomatosis does not occur in children only, as stated by Christian and Hand, but also frequently in adults. Cases are reported by Alberti, at 21 years; Hochstätter and Veid, 44 years; Schüller and Chiari, 26 years; Chester, at 44 and 69 years; Kartagener and Fischer, 21 years; Dalitsch, 30 years. Most of the cases the roentgenologist will get from the paediatrician and from the internist, with the symptoms of exophthalmos and diabetes insipidus, and eventually other symptoms of dyspituitarism, such as dystrophia adiposogenitalis, dwarfism in adults, Simon's cachexia. The patients may come with all the symptoms, with some, or with one, or even without any. A case may be sent by the surgeon for examination of a simple fracture, and he may find a pathological fracture in a cystic, changed, bone. He may get a patient from the dentist with non-typical stomatitis, gingivitis, loosening and loss of teeth, for examination of the roots of the teeth, and will find decalcification and defects in the jaw, or cysts at the tip of the root resembling granuloma or sometimes even epulis. The otologist sends a case with deafness and discharge from the ear for a picture of the petrous bone and the mastoid, and he finds extensive non-typical decalcifications. Or he may find accidentally a stippled lung field like miliary tuberculosis without clinical complaint. In all these cases, the roentgenologist has to think of xanthomatosis; then xanthomatosis will not be so rare a disease in the future.

#### TREATMENT

The only effective treatment is x-ray irradiation. The results of x-ray therapy are reported by Cignolini,<sup>15</sup> Vampre, Schüller, Rothman, Sosman, Kartagener and Fischer, and Dalitsch. Cignolini was the first to try x-ray therapy in a case of Schüller-Christian disease in the year 1928.

His patient, a boy of 14, was examined because of loss of teeth, gingivitis and stomatitis. The x-ray picture showed cystic areas in the jaws. An additional examination of the whole skeleton was made and revealed typical defects in the cranial vault, the os ilia, the femora, and the ribs as well.

The history of the case disclosed that the patient had suffered for 12 years with diabetes

insipidus, and had been treated with parathyroid and with pituitary gland extract. He showed under-development and under-nourishment; puberty had not developed. Cignolini administered half an erythema dose to the right jaw; three days later he administered half an erythema dose on the left jaw and repeated the same dose one month later. Improvement was evident after three weeks. The gingivitis and stomatitis disappeared and the teeth, which were almost falling out, became almost normal. He also tried a cautious irradiation of the hypophysis with  $\frac{1}{4}$  HED. The effect was still more striking. While before the patient consumed ten to twelve litres of fluid daily without pituitary injection and six to seven litres with daily pituitary injections, after the irradiation the daily consumption of fluid decreased to the normal amount of 1.5 litre to 2.5 litres without any pituitary injection. Further, the small patient grew 8 cm. in a few months and puberty developed. The other bone defects were irradiated with half an erythema dose. The same doses were repeated after one month and after three months. Defects in the bones healed and an almost normal structure of the bone was restituted.

Vampre's patient was a boy 15 years of age, in whom 11 years before the diagnosis of chloroma had been made. He showed exophthalmos, polyuria (to 25 litres daily) and hypogenitalism. After irradiation he showed increase in growth and normal sexual development. The diabetes insipidus decreased to 6 to 7 litres daily. Exophthalmos was not influenced. The effect of the irradiation on the defects of the bones is not reported.

Schüller and Chiari report a good effect from x-ray in their case, but they do not give any details of the treatment. Rothman's patient was a boy 2 years of age with defects of the bones in the skull, in the scapula, in the ribs, the humerus, the femur, and eczema of the skin. Under x-ray therapy, the eczema healed and the defects in the bones began to heal. The patient died suddenly. There was no autopsy.

Sosman treated his patients with 185 kv. peak, 40 cm. skin focus distance, with a 0.5 mm. copper filter. He gave a total dose of 646 r (85 per cent erythema dose). These total doses he divided into two equal portions (323 r) and administered them with an interval of two to seven days. This dose naturally causes epilation. Later he decreased the doses 250 r, to 200 r, which amount did not cause epilation. The effect Sosman reports as follows. One-third of an erythema dose was administered to the right frontal area on March 5th and March 8th. X-ray examinations, six weeks and three months

later, showed definite healing of the defects in the right frontal area, while the non-treated defects in the left parietal bone had increased in size.

The patient of Kartagener and Fischer was a man 21 years of age, with diabetes insipidus, exophthalmos, defects in the bones of the skull, in the vault and in the base. The jaws were reduced to a narrow strip of chalk (calcium); there were defects in the bones of the pelvis, ribs, and in the long bones. The x-ray picture showed the typical small spotted (stippled) lung, as in miliary tuberculosis. The treatment was carried out by Prof. Schinz. He applied three times 300 r to each focus in the bone, using a tension of 160 kv. peak and a filter of 0.5 mm. copper, *halbwertschicht* in copper, 0.58 mm.; target skin distance was 40 cm. The left lung only was irradiated and the right semi-thorax strictly covered, to control and compare the effect of the irradiation with the non-treated side. Five treatments of 240 r each were applied to the back of the left semi-thorax and the same amount to the front of it, making a total of 2,400 r. In the irradiation of the lung 180 kv. peak and 1 mm. copper filter was used. *Halbwertschicht* was 1.1 mm. copper, skin focus distance 63 cm. X-ray therapy was begun on December 12, 1930, and was continued until May 23, 1931, when the patient was discharged. The pathological changes in the lungs and in the long bones were unaltered. On the other hand, the x-ray picture of the skull showed a distinct decrease of the defects. The x-ray finding of the jaw was unchanged, and the base of the skull was found equally unchanged.

Finally Dalitsch reports the good effect of x-ray treatment in a case of xanthomatosis in an adult patient. Rowland, who was the first to discover the correct nature of xanthomatosis, and has observed many cases of his own, in a personal interview expressed the opinion that the changes do not respond to x-ray treatment; at least he did not see any benefit from it, but an illusion of effect is produced by spontaneous remissions which occur very frequently in this disease. He showed many x-ray pictures with spontaneous remissions until definite healing and normal structure of the bone, and x-ray pictures of treated cases without any changes in the defects resulting.

#### SUMMARY OF THERAPY

It is difficult to judge the value of x-ray treatment because of frequent spontaneous remissions in the disease. Further observations are still necessary. But apparently acute gingivitis and loosening of the teeth respond best to x-ray treatment. The hypophysis also responds well if it is not entirely destroyed by lipoid granuloma, but it is hindered in its function. The diabetes insipidus decreases; development and puberty, if disturbed, become normal. Next to respond to the treatment are the defects in the skull. The changes in the long bones also respond well, but not so promptly as the changes

in the cranial vault. The changes in the lung apparently do not respond at all; at least the x-ray picture of the lung is unchanged. This fact may be explained because the changes in the x-ray picture are not produced by an accumulation of xanthoma cells in the lung but by a secondary fibrosis, namely, by multiple small nodules consisting exclusively of connective tissue, which properly are scars after lipoid granuloma. But is it possible, in spite of the unchanged x-ray finding, that the recent, not yet fibrosed, lipoid granulomatous focus reacts well to irradiation, and the progressive fibrosis of the lung is arrested? It is possible, we think, that x-ray treatment of the lung meets a vital indication, although no result of the treatment is to be seen in the picture. It has to be considered also that one x-ray treatment of the lung has been observed only, and this in an adult patient who did not respond in general very well to the treatment.

Xanthomatosis in adults does not seem to respond as well to x-ray treatment as in children; either because the power of regeneration of the growing organism is greater, or because xanthomatosis of adults is of longer duration and is characterized by more secondary fibrosis which is resistant to x-ray irradiation. By all means it is desirable that xanthomatosis of the lungs should be treated with x-ray and the results reported. A greater amount of material will enable one to give a definite opinion.

#### TECHNIQUE

Use deep therapy tension of 160 to 180 kv. peak and heavy filter of 0.5 mm. copper. For superficially situated changes in the bone, as in the cranial vault, use lower tension, 120 kv. peak and lighter filter, 4 mm. aluminum. Apply to each focus in the bone twice 200 r to twice 250 r, with an interval of one week, measured on the patient. If there is no improvement after two months, and the x-ray control does not show any decrease in the lesions, repeat the series with three times 200 r to three times 250 r in one week, and so on, up to the limit of the tolerance of the skin. Treat the foci in the bones, each separately, one after another, and examine the blood. Treat gingivitis and loosening of teeth with irradiation of the bone of the jaw and use a similar dose. For treatment of the hypophysis, use four areas of skin and apply 150 r to each on four consecutive days. If the patient does

not respond to this dose, increase to the limit of the tolerance of the skin. There is no danger of further damaging by x-rays the already disturbed function of the hypophysis, because the hypophysis has been proved to be very resistant to x-ray. In the treatment of tumours of the brain, where the hypophysis has also been irradiated with the largest doses, no damage of the hypophysis by x-rays has been observed. It was also found impossible to disturb the function of the hypophysis of a dog by x-ray irradiation with large doses (Sosman). There is no sufficient experience with irradiation of the lung to recommend any technique in regard to it. Try the above mentioned technique of Prof. Schinz, 240 r five times to the back and to the front. Treat each hemi-thorax separately, first, to control the effect of the treatment and to compare it with the other side, and, secondly, in order not to irradiate too large a skin area at once. With children use slightly less dosage. Frequent examination of the blood is most important here, because large areas of the body are irradiated. It has to be considered also that the normal lung reacts sometimes with extensive fibrosis on x-ray irradiation, as has been observed by the chief of our clinic, Dr. A. H. Pirie, in several cases of carcinoma mammae treated with deep therapy. In judging the results of the x-ray treatment you must not forget that spontaneous remissions occur very frequently in xanthomatosis, and that the defects may disappear entirely.

Therapy other than x-ray has proved entirely ineffective. The results with low fat and cholesterol diet reported by Rowland could never be repeated in any other case. Treatment was also tried with parathyroid, calcium and vigantol, because of the extensive decalcification of the bone; insulin (twice 5 units daily), and thyroid to lower the cholesterol level of the blood. Injections of pituitary influence the diabetes insipidus, but they do not influence the changes in the bone, because these are primary and the dyspituitarism is the consequence only of their accidental localization in the sella.

#### PROGNOSIS

Since xanthomatosis is a granuloma and not a tumour, the prognosis is not hopeless. The patient described by Christian in 1919 is still alive, studying at college. The patient first described by Schüller is also still alive; the de-

fects in the skull have disappeared, but the diabetes insipidus still exists. The mortality in this disease is about 30 per cent. Especially endangered are those with infiltration of the lungs, because the secondary fibrosis often causes insufficiency of the right heart. The disease shows a prolonged course of decades with many spontaneous remissions.

#### PATHOGENESIS

Rowland adopts the opinion of Pinkus and Pick<sup>16</sup> that the xanthoma (lipoid-granuloma) of the skin is produced by a primary increase of the lipoids in the blood serum; the same for the Schüller-Christian disease. This opinion has since been shared by all other authors. See Sosman.<sup>17</sup> This theory of Rowland has been further developed by Brahm and Pick,<sup>18</sup> who say that it is a disturbance in the cholesterol metabolism in contrast to the Niemann-Pick disease which is a disorder of the phosphatide metabolism (lecithin) and Gaucher's disease which is a disorder of the kerasin metabolism. Pick thus has drawn up the following Schema of the lipoid metabolism diseases.

*Primary disorders:* (1) morbus Christian-Schüller—disorder of the cholesterol metabolism; (2) xanthomatous eruption of the skin—also disorder of the cholesterol metabolism; (3) morbus Niemann-Pick—disorder of the phosphatide metabolism, mainly lecithin; (4) morbus Gaucher—kerasin disorder of the metabolism.

*Secondary disorders:* in jaundice, diabetes.

A summary of the cholesterol tests of the blood in the cases observed until now gives the following result. The cholesterol level of the blood was increased:

Hofer, 238 mg. per cent; Sosman, second case, 185 mg. per cent; Chiari, 192 mg. per cent; Hochstätter, 174 mg. per cent; Weidman and Freeman, 397 mg. per cent.

The cholesterol level of the blood was normal or sub-normal in the following cases:

Sosman's third case, 84 to 165 mg. per cent; Chester, 95 mg. per cent; Kartagener and Fischer, 148 to 164 mg. per cent; Kienböck and Schneek, 140 mg. per cent; my own case, 140 mg. per cent.

Eight cases of Schaaf and Werner with xanthomatosis of the skin:

One case—increased cholesterol content of the blood; three cases—normal cholesterol level; four cases—sub-normal.

The normal cholesterol level of the blood is about 140 mg. per cent before a meal.

Since hypercholesterolemia is otherwise not

so rare, it appears that it is not more frequent in xanthomatosis than in people without xanthomatosis. In this way, the theory of Rowland, that xanthomatosis is caused by a primary cholesterinæmia, is not to be proved. In addition, the attempts to cure xanthomatosis with a low cholesterin and fat diet, as has been recommended by Rowland, have not succeeded. Likewise, the attempts to influence the xanthomatous infiltrations by lowering the cholesterin content of the blood with insulin and thyroid injections were not effective.

But a disorder of the cholesterin metabolism is not necessarily hypercholesterinæmia. The observations of Spranger, Werner and Schaaf suggest the following theory. Xanthomatosis is caused by a disorder of the balance of the fat emulsion in the serum, which causes a separation of cholesterin and fat drops, and deposits the cholesterin in the tissues. Fats are kept emulsified in the serum by cholesterol and its esters. According to the *in vitro* experiments of Spranger, the optimum for the emulsion of fat in water is achieved by a cholesterol-cholesterol-ester index of 40:60. In serum the cholesterol-cholesterol-ester index is about 30:70. If new fat is introduced into the blood the blood adapts itself by increasing its emulsifying power, changing the relation between cholesterol and cholesterolester till the stability of the fat emulsion is restored as it was before. But if the blood loses its ability to adapt itself to increased new fat intake, the newly introduced fat separates itself from the blood, drawing with it part

of the fat and of the cholesterin content of the blood. The Bürger test<sup>18</sup> is based on this theory. Test the total fat and cholesterin in the blood before a meal. Give 5 g. of cholesterin in 100 c.c. of olive oil, and test the blood after two, eight and twenty-four hours. Normally, the cholesterin content of the blood increases to double its amount (to 280 mg. per cent). Pathological cases with a disorder in the fat balance show a paradoxical reaction. After the intake of cholesterin, the cholesterin content of the blood, as well as the total fat, decreases greatly. Schaaf and Werner proved a similar reaction in 7 cases of xanthoma with a normal and subnormal cholesterin content in the blood. In the case of Kartagener and Fischer of the Schüller-Christian syndrome, with a cholesterin content in the blood of 140 mg. per cent, their examination had the following result (see attached Table on the Bürger test), which proves that xanthomatosis is not caused by excess of cholesterin content in the blood as Rowland suggested, but by a disorder in the stability of the fat emulsion in the blood. The opinion is correct that xanthomatosis is caused by a disorder of the cholesterin metabolism. The genesis by a disturbance of metabolism does not change the specific granulomatous nature of this particular disease.

#### SUMMARY

Xanthomatosis is a specific granuloma which is not caused by microorganisms, but by a disturbance in the stability of the emulsion of cholesterin and fat in blood. There is no hyper-

BÜRGER TEST  
(AFTER 5 G. OF CHOLESTERIN AND 100 G. OF OLIVE OIL)

	Total Fat Extract Mg. Per cent	Phosphatide Phosphorus Mg. Per cent	Lecithin Mg. Per cent	Cholesterin			Ester Per cent of Total Cholesterin
				Total Mg. Per cent	Free Mg. Per cent	Estered Mg. Per cent	
<i>First Test:</i>							
Before fat meal . . . . .	770	10.6	266	148	35	113	76.4
4 hours after fat meal . . . . .	825	10.1	252	118	32	86	72.8
8 " " " "	645	9.7	242	143	24	119	83.2
24 " " " "	650	9.7	242	116	34	82	70.6
<i>Second Test:</i>							
Before fat meal . . . . .	1285	7.25	182	164	48	116	70.8
1 hour after fat meal . . . . .	1305	10.05	252	144	43.5	100.5	69.7
2 hours " " " "	1230	9.2	230	174	56	118	68.4
4 " " " "	1020	9.8	246	171.5	53.5	118	68.7
8 " " " "	890	11.0	277	115.5	41.5	74	64.0
24 " " " "	800	8.35	210	124	40	84	67.7

This analysis shows that the fat meal was absorbed, but in spite of this the total fat and the cholesterin went down.

cholesterinæmia. It is suggested that the name "xanthoma", which connotes "tumour", be changed for "lipoid granuloma". Xanthomatosis is defined as general infiltration with lipoid granuloma. The Schüller-Christian disease is subordinated to xanthomatosis instead of being identified with it. Therefore, in my title "xanthomatosis" and "Schüller-Christian syndrome" concerns those cases with defects in the skull and dyspituitarism only.

The x-ray diagnosis, differential diagnosis, treatment and prognosis of the disease are given.

One case of Schüller-Christian disease of my own observation is reported.

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#### COMMON DUCT OBSTRUCTION WITH LIPIODOL STUDIES OF CHOLANGIECTASIS AND THE EFFECTS OF PROLONGED DRAINAGE\*

BY P. H. T. THORLAKSON, M.D., C.M., M.R.C.S. (ENG.), F.R.C.S.(C.),

*Lecturer in Clinical Surgery, Faculty of Medicine, University of Manitoba,*

AND

J. C. McMILLAN, M.D., F.R.C.P.(C.), F.A.C.P.,

*Lecturer in Medicine (Roentgenology and Electro-Therapeutics)*

*Faculty of Medicine, University of Manitoba,*

*Winnipeg*

DILATATION of the intra-hepatic biliary tract as a result either of calculus or of cicatricial or neoplastic obstruction of the common bile duct has long been recognized and has been referred to as "cholangiectasis". The obstruction leads to a damming back of the bile, and this, in conjunction with co-existing infection, brings about the following changes, *viz.*, a cylindrical dilatation of the common duct and the hepatic ducts, sacculation of the intra-hepatic biliary system, pressure atrophy of the

parenchymatous liver cells, interference with the portal circulation, cholangitis, hepatitis, and, finally, a general fibrosis of the whole liver, with great impairment of function. The degree and permanence of the functional damage to the liver depend upon the duration and the completeness of the obstruction and the virulence of the infection. The purpose of this paper is to show radiographically the structural changes in the biliary tree in patients suffering from common duct obstruction of varying degree, and to demonstrate the improvement which follows prolonged drainage or drainage with irrigation of the bile passages.

In reviewing the literature on common duct

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dilatation one finds many interesting observations. In 1932, Zinner and Cash<sup>1</sup> published an exhaustive report on congenital cystic dilatation. They reported a case of their own and found previous reports of 82 cases in which the records justified the diagnosis of congenital cystic dilatation of the common duct.

Dilatation of the biliary passages has been produced experimentally by many observers, and its effect on the liver economy studied. McMaster, Broun, and Rous<sup>2</sup> reported observations on the changes in the biliary tract following obstructive lesions, and suggested the term "hydro-hepatosis". They demonstrated that the character and colour of the bile depended upon the functional activity of the gall-bladder. If the concentrating and absorptive power of the gall-bladder is normal the bile is dark and thick; if the gall-bladder is not functioning the ducts are filled with so-called "white bile", mostly mucus secreted from the duets, the bile pigments having been re-absorbed.

An outstanding article by Counsellor and McIndoe<sup>3</sup> demonstrated the structural changes which occur in different types of biliary disease. It is illustrated by beautifully prepared casts of the biliary tree in 26 post-mortem specimens. Ten cases had no biliary tract disease and acted as controls. They made careful measurements of the different branches of the duct system and showed the degree of dilatation present. In 8 cases there were stones in the gall-bladder, not suspected before autopsy, and 7 of these showed general duct enlargement. The degree of dilatation seemed to correspond to the severity of the infection and damage found in the wall of the gall-bladder itself. In 3 cases where cholecystectomy had been performed within ten days of death, all showed dilatation of the intra-hepatic bile ducts. In 5 cases in which the obstruction of the common duct was caused by benign stricture or malignant growth the degree of dilatation was marked and the parenchymatous liver damage extensive.

The use of lipiodol as a means of visualizing the bile passages is of quite recent date. Our observations were original with us, but review of the literature showed that somewhat similar work has been carried out by others. However, we can find no record of a series of studies illustrating the changes that occur in severe cases during the course of treatment, especially showing the marked improvement in the intra-

hepatic biliary system which results from prolonged drainage. Gabriel<sup>4</sup> in 1930 published an article on "Proof of patency of the common bile duct by the injection of lipiodol". R. H. Overholz<sup>5</sup> in 1931 reported "Biliary tract visualization with radiopaque oil". Ginzburg and Benjamin<sup>6</sup> in 1930 presented a series of "Lipiodol studies of post-operative biliary fistulae". Lahey<sup>7</sup> in 1932 reported similar work, and recently Judd and Phillips<sup>8</sup> have presented a series of cases entitled "The patency of the biliary ducts".

Ginzburg and Benjamin state that in the absence of obstruction distal to the internal opening of the biliary fistulous tract the lipiodol appears almost immediately in the duodenum, and there is no reversal of flow up into the intra-hepatic biliary radicles, and, further, that the presence of obstruction will prevent the entrance of lipiodol into the duodenum and will result in reversal of flow if sufficient lipiodol is used. It is to be noted that these observations were conducted on patients with external biliary fistulae, whereas our observations were made on patients in whom the hepatic arm of the T-tube was lying within the lumen of the common duct.

In our cases the lipiodol passed into the duodenum without delay, but it also ran up into the duct system and outlined the intra-hepatic biliary tree, in spite of the fact that there was obviously no distal obstruction. We feel that *failure to visualize the intra-hepatic system depends upon a widespread cholangitis, and that this cholangitis subsides following prolonged drainage, or drainage and irrigation.* As illustrated by Case 5, the intra-hepatic system will be visualized well as soon as the ducts are cleared of the viscid stagnant contents, and thus visualization indicates improvement following drainage and not necessarily obstruction, as they point out.

#### RADIOGRAPHIC TECHNIQUE

The foot of the x-ray table (Bucky) is elevated about six inches, in order that gravity may assist the flow of lipiodol into the liver duct system. (This is probably not necessary). The apparatus is set ready to take the x-ray film. A 20 c.c. syringe full of lipiodol is attached to the end of the T-tube, and the oil is injected with a slow steady pressure on the piston of the syringe, taking about 30 to 45 seconds for

the complete injection. The first plate is taken immediately upon completion of the injection. A second plate is taken 20 minutes later.

The following are summarized histories of 5 cases which form the basis of this report, together with the x-ray pictures in each case.

#### CASE 1

Mrs. A.C.S. Our first observations were carried out upon a female patient whose pre-operative history was briefly as follows. She had had jaundice, which was constant but varied in degree, and repeated colic, associated occasionally with chills. These manifestations followed a cholecystectomy done 18 months previously. The icterus index was 52.

The usual pre-operative preparation of blood transfusion, intravenous calcium chloride, and repeated injections of intravenous glucose, was given. At

operation the supra-duodenal portion of the common duct was found to be replaced by an elongated narrow stricture. Above the stricture the common duct was dilated, and both right and left hepatic ducts contained a great deal of biliary mud and many calculi. The duct was repaired over a T-tube. The immediate post-operative course on the whole was uneventful, but the jaundice was slow in subsiding. The biliary passages were irrigated with warm normal saline three times a week after the first week. With each lavage some fine biliary sand and large quantities of mucus came through the tube, indicating the presence of widespread catarrhal cholangitis and stagnation in the sacculated portion of the intra-hepatic ducts.

On the 30th day after operation, 20 e.c. of lipiodol were injected through the T-tube, first to determine the patency of the lower portion of the common duct and to observe the speed with which the opaque solution passed on into the duodenum, and, secondly, to demonstrate, if possible, the presence of any calculi in the ducts that might have been overlooked at the

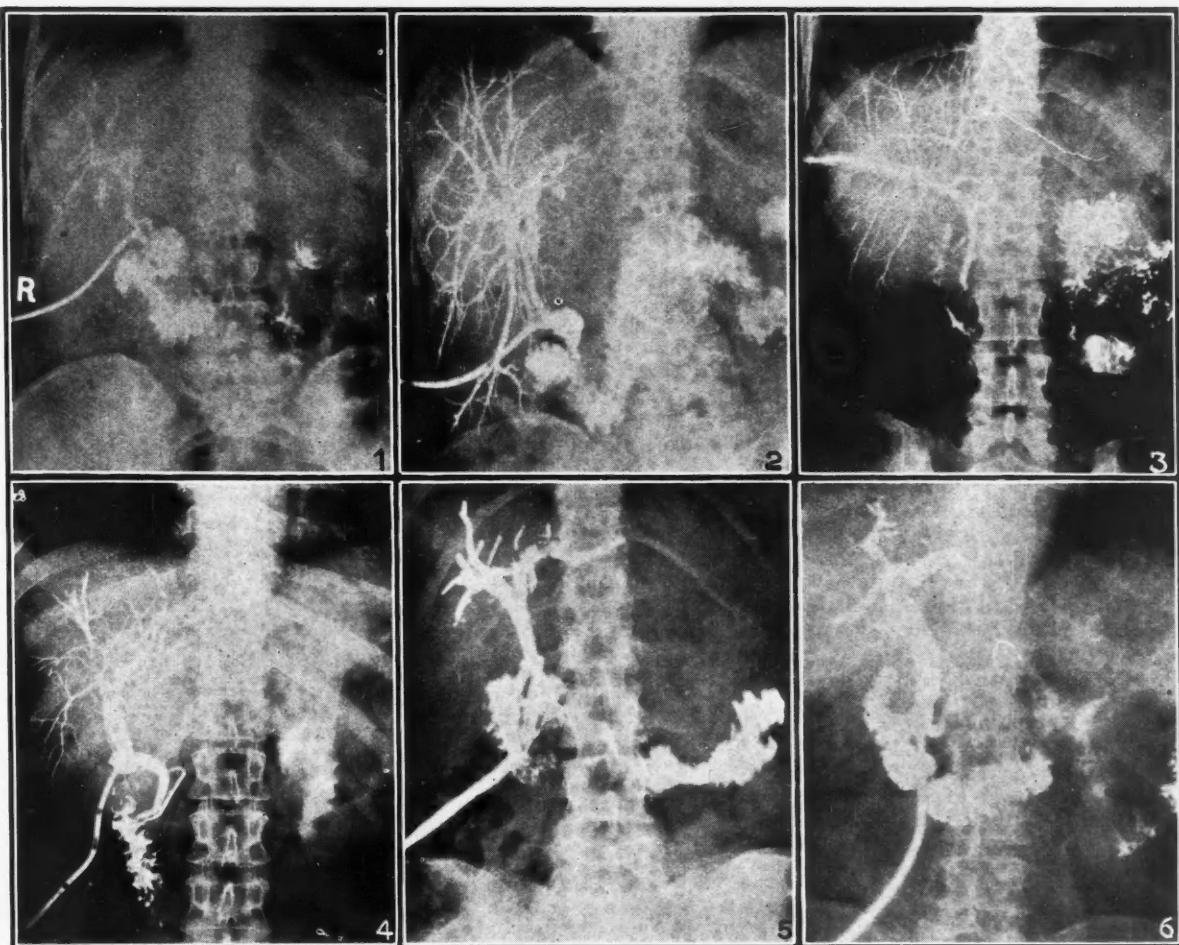


FIG. 1, Case 1 (June 10, 1933).—Marked dilatation of common and hepatic ducts. The hepatic ducts at operation were found to contain large amounts of thick mucus and sand. Very few of the smaller ducts are visualized.

FIG. 2, (Oct. 2, 1933).—Same case as Fig. 1 (3½ months later) showing marked improvement following drainage and irrigation, and excellent visualization of the outermost radicles of the intra-hepatic biliary duct system. The clinical course of this case showed a corresponding improvement.

FIG. 3, Case 2 (June 8, 1933).—Normal biliary tree. No dilatation of the ducts, and excellent visualization of the finer radicles.

FIG. 4, Case 3 (June 2, 1933).—A slight degree of dilatation of the biliary ducts, with non-visualization of the outermost radicles.

FIG. 5, (Aug. 3, 1933).—Moderately advanced dilatation with non-visualization of the greater portion of the intra-hepatic duct system.

FIG. 6, Case 5 (Oct. 4, 1933).—Marked dilatation of the common and hepatic ducts, with practically no visualization of the intra-hepatic ducts.

time of operation. As illustrated in Fig. 1 the opaque solution passed rapidly on into the duodenum and upper jejunum, but only the common and lower dilated and sacculated segments of the hepatic ducts were visualized. We interpreted this as confirming our clinical suspicion that the intra-hepatic biliary tree was filled, and probably plugged, by the products of a chronic biliary inflammation. The drainage and irrigations were continued and the jaundice gradually improved, though there were occasional exacerbations with slight fever, indicating persistent intra-hepatic infection. During the next three months the patient improved so much that at times she was jaundice-free and the irrigations had for some weeks failed to wash out sand and mucus. Fig. 2 illustrates the marked improvement that occurred in the intra-hepatic biliary tree during this period. A comparison between this x-ray plate and that of Fig. 1 shows that now even the finer radicles of the biliary passages are unobstructed. These two plates also demonstrate that the liver is enlarged, and that the intra-hepatic ducts are undoubtedly permanently damaged and dilated. The rapid emptying of the opaque solution into the bowel below indicated that there was no obstruction to the flow through the common duct.

#### CASE 2

Miss M.R., aged 32. This patient was referred to us because of the fact that she was having repeated attacks suggesting biliary colic (pain, tenderness, and marked rigidity in the upper right quadrant with referred pain to the right subscapular area, and vomiting). Her gall-bladder had been removed previously. There was no history of jaundice, and the icterus index taken during the attack was normal. A thorough investigation proved negative, including a blood Wassermann test. Several consultations were held and she was placed on rigid medical management, without relief. After going into the details of her history and three laparotomies (appendectomy, cholecystectomy, and Finney), we finally decided to explore the common duct. This appeared normal as to size and thickness, and a probe passed easily into the duodenum. The liver appeared perfectly normal. However, in view of the history and the fact that palpation of the pancreas revealed slight evidence (?) of chronic pancreatitis a small T-tube was placed in the common duct. The patient received absolutely no benefit from this procedure, her pseudo-biliary colic persisting with the tube in the duct. Before withdrawing the T-tube, 20 c.c. of lipiodol were injected, showing not only a perfectly normal biliary tree, but also rapid passage of the lipiodol into the intestine. The lipiodol can be followed into the outermost radicles of the bile ducts. The fact that we are able to demonstrate, radiographically, what we consider to be a normal biliary tree (Fig. 3) is thereby explained.

#### CASE 3

Mrs. D.D.R., aged 32. The history revealed that a gall-bladder containing calculi had been removed a few months before admission to hospital. Since the operation the patient had suffered a few attacks of colic and jaundice, without temperature, the jaundice subsiding rapidly. With some of the attacks no jaundice had been noted. A pre-operative diagnosis of common duct stone was made. At operation a stricture of the common duct was found at the site where the cystic duct had been ligated; the common duct otherwise was free. The stricture was repaired over a T-tube. Fig. 4 shows the biliary tree three weeks after operation, and illustrates the earliest changes that we have been able to observe. Comparison with Fig. 3 shows that the finer radicles of the ducts are not visualized. There is slight evidence of dilatation. One of the pancreatic ducts is visualized. The opaque medium entered the duodenum without

delay and a film taken 20 minutes subsequent to injection showed almost complete disappearance of the opaque solution from the bile passages.

#### CASE 4

Mrs. A.T., aged 35. This patient gave a long history of flatulent dyspepsia and slight pain, but no jaundice until six weeks before operation, when she suffered from an attack of severe obstructive jaundice with fever and pain. She was tided over this attack. Six weeks later, at operation, a thickened inflamed gall-bladder full of calculi was found. The common duct was dilated and contained several calculi with considerable biliary mud. The common duct was drained by means of a T-tube. Fig. 5 illustrates a case with dilatation of the common, right and left ducts, and slight visualization of the intra-hepatic biliary passages. The branches of the biliary tree are cut off closer to the main ducts. This corresponded very closely to this patient's clinical history.

#### CASE 5

Mrs. L.O., aged 55, had suffered from attacks of epigastric pain for 28 years. She had never been jaundiced. The attacks of pain lasted from 20 to 30 minutes. We were unable to elicit the slightest tenderness in the gall-bladder region, though she was examined immediately after an attack. Her temperature was normal. X-ray investigation revealed the presence of a traction diverticulum of the second part of the duodenum, and the gall-bladder failed to be visualized. At operation a dense mass of adhesions was encountered over the region of the gall-bladder. A small, contracted, thickened gall-bladder was found. The duodenum was adherent and had been tented up by the contracting gall-bladder. The common duct was dilated and contained two calculi and a large amount of yellow-coloured mud. This material was scooped out and the duct washed out with normal saline. T-tube drainage was provided. Visualization of the biliary tree four weeks after operation revealed marked dilatation of the common, right and left bile ducts. Fig. 6 shows the branches of the biliary tree cut off still closer to the main ducts. The dye drained freely into the duodenum.

Our interpretation of the cases showing incomplete visualization of the biliary tract is that the finer radicles are filled with tenacious infected mucus which prevents the lipiodol from spreading freely throughout the smaller bile passages. We feel that in such cases irrigation of the ducts with warm normal saline is indicated, and that this procedure, if carried out with ordinary aseptic precautions, is not attended by any ill effects.

#### SUMMARY

1. Five cases are presented to show the possibility and the value of x-ray visualization of the biliary passages in common-duct obstruction after drainage has been established.
2. Examination and comparison of the x-ray plates shown illustrate that the x-ray evidence of dilatation of the main ducts and the varying degrees of obstruction of the intra-hepatic biliary passages correspond very closely to the

clinical history and operative findings in each case.

3. This method of investigation is of value in demonstrating the patency of the ampulla of Vater, and in severe cases provides a radiographic record of the improvement that occurs in the smaller intra-hepatic bile ducts during the course of drainage.

4. No toxic symptoms have been noted in any of our cases from the lipiodol. In one case 40 c.c. of lipiodol were injected without any harmful effects.

5. One of us (J.C.McM.) was struck by the radiographical similarity between this condition and bronchiectasis. Taking into consideration also the nature of the retained secretions within the dilated and sacculated ducts in the presence of infection, we feel that the term "cholangiectasis" is more appropriately descriptive of the condition than the term "hydro-hepatosis".

6. The cases presented in this paper illustrate one type of cholangiectasis. There is another form which develops as a result of gradually increasing obstruction such as we have with carcinoma of the head of the pancreas. In this

condition both extra- and intra-hepatic ducts become enormously enlarged and sacculated. As the obstruction becomes complete the contents of the bile passages are altered and instead of bile we encounter a watery mucinous material. Infection is absent or is a negligible factor in these cases. There are, therefore, two distinct types of cholangiectasis met with by the surgeon in dealing with common duct obstruction. We propose the following nomenclature to describe these types: (1) Chronic non-infective cholangiectasis (mucinous). (2) Chronic infective cholangiectasis (calcareous).

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## GONOCOCCAL ENDOCARDITIS\*

By W. W. EAKIN, M.D., F.R.C.P.(C.),

*Montreal*

THE cardiac complications of gonococcal infection are well known—a general septicæmia causing an endo-, myo- or peri-carditis. The fever is high, remittent in type, and embolic phenomena are common. The average duration of the illness is four to ten weeks. In contrast to the prevalence of urethritis, however, it would appear to be of rare occurrence; as yet there are less than 100 proved cases reported in the literature.

In a review in 1922, Thayer<sup>1</sup> reported 72 cases of gonococcal endocarditis which had appeared in the literature. To these he added 12 of his own. His conclusions were that it was a grave, though not an infrequent malady; in 176 cases of acute endocarditis of determined origin, 20, or 11.3 per cent, were gonococcal in origin. The aortic valve in his own series was

the one most frequently involved; the pulmonary next, the predominance of aortic involvement being greater in all the reported cases, forming 70 per cent.

In 1932, Hoffman and Taggart<sup>2</sup> discarded some of the cases which had previously been reported, on the grounds of insufficient diagnostic evidence. These authors added another case and reviewed 8 others which had subsequently been reported; they state that the total number reported is 76 proved cases. They agree with Karsner<sup>3</sup> that the diagnostic criteria must demonstrate the presence of gonococci in the blood or lesion, to be accepted as such.

In this hospital, during the past 16 years, of 91 cases of acute bacterial endocarditis, 4 were gonococcal in origin, though 2 must be discarded as not being proved. One of these was that of a girl of 18 who developed an acute vaginitis, and one week later gonococcal arthritis and endo-

\* From the Department of Medicine, McGill University Clinic, Royal Victoria Hospital, Montreal.

carditis. Autopsy revealed an ulcerative endocarditis of the mitral valve, ulcerative arthritis of the right knee joint, an exudative purulent arteritis of the left common iliac artery together with thrombus formation at the lower end of the aorta and the beginning of the right and the left common iliac arteries. Blood cultures during life were negative, and bacteriological studies at autopsy did not demonstrate gonococci.

The other two cases were both detected in 1933 and are herewith reported.

#### CASE 1

A male, aged 29 years, a hairdresser.

*Complaints.*—Chills. Palpitation. Gonorrhœa for five months.

*History of illness.*—The patient was perfectly well until June, 1933, when, three to four days after exposure, he developed gonorrhœa. He consulted his physician who prescribed urethral injections, which were to be retained for ten minutes. In three to four weeks he was greatly improved, the discharge lessened, and the injections were used only twice daily. During the following three months there was no dysuria and the discharge was noted as only a small drop in the morning. At the end of August, 1933, he was considered cured. During this time, he had felt well. Within a few days, however, the discharge reappeared and he consulted another physician who gave him prostatic massage and irrigations twice a week. On September 20, 1933, he developed an orchitis on the left side. Caprikol capsules were given, the patient remained in bed, and the swelling gradually disappeared. Two weeks later, prostatic massage and irrigations were recommenced. Shortly after returning to work, early in October, 1933, he noticed the occurrence of chills. These occurred twice a day, usually in the morning about eleven o'clock, and would last two to three hours, following which he would perspire a great deal. During this time, the patient felt weak, but he attributed this to his stay in bed and to the fact that he had developed a "cold". He stated, however, that since September 1st he had been losing weight, had suffered from occasional night sweats and malaise, and also had noticed progressive pallor. He continued at work however, until the latter part of October, when he took to bed, complaining of chilly sensations and palpitation. At this time an aortic murmur was noted, which, during the following days appeared to increase in intensity. He was seen in consultation on November 2, 1933, and was admitted to this hospital.

*Family history.*—Irrelevant.

*Personal history.*—He had had mumps, scarlet fever and influenza some years previously. There was no history of rheumatic fever, tonsillitis, or of heart disease. He had had a previous attack of gonorrhœa in 1929, which, he stated, cleared up in three weeks' time.

*Physical examination* on November 2, 1933, showed no acute distress. There was a marked pallor of the skin. There was no clubbing of the fingers, and no petechiae were present. Marked pulsation in the carotid arteries and capillary pulsation was observed. There was no evidence of increase in venous pressure; no œdema. Temperature, 104°. The pulse was regular, collapsing in character; no arterial thickening. Blood pressure 100/30; equal in both radials.

Over the apex and mid-precordium a short presystolic thrill was palpable. The heart was not enlarged. The sounds were of good quality, well heard

at all areas. At the apex a rough presystolic murmur lead up to an accentuated first sound, which, in turn, was followed by a blowing systolic murmur transmitted to the axilla. At the base, and most intense over the aortic area, blowing systolic and rough diastolic murmurs were heard, the latter transmitted to the vessels of the neck and down the left border of the sternum.

The lungs were clear. The liver and spleen were not enlarged. The left testicle was slightly enlarged. The prostate per rectum was not enlarged or tender. A smear from the prostatic fluid showed no gonococci.

*Laboratory examination.*—Urinalysis.—The urine showed a specific gravity of 1024. Neither albumin nor sugar was present. Microscopic examination revealed nothing abnormal. Two days before death, a heavy trace of albumin was noted for the first time.

Blood count.—Red blood cells 3,350,000; white blood cells 11,200; haemoglobin 51 per cent. Blood Wassermann test, negative; gonococcal fixation, 4 plus. Blood culture.—(By Dr. D. H. Smith, of the Department of Bacteriology). After several negative results, gonococci were isolated on blood culture.

X-ray film, made at six feet, showed the heart to

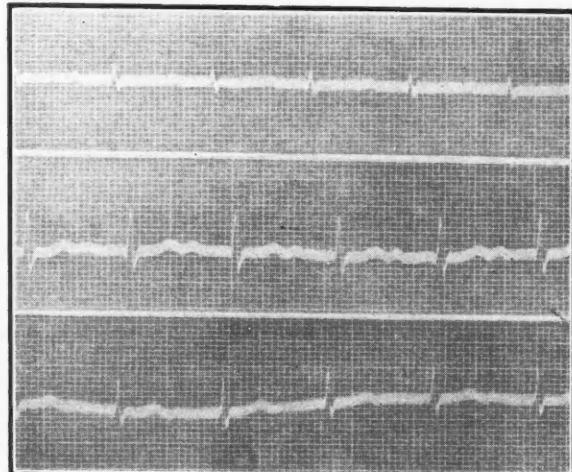


FIG. 1. Case 1.—Electrocardiogram showing definite prolongation of the P-R interval. 0.28 secs.

be normal in size and shape (mid-left diameter 9 cm.; mid-right 4 cm. Internal diameter of the thorax, 25.5 cm.). The aorta and diaphragm appeared to be normal. The lung fields were clear.

The electrocardiogram (Fig. 1) showed definite prolongation of the P-R interval (0.28 seconds).

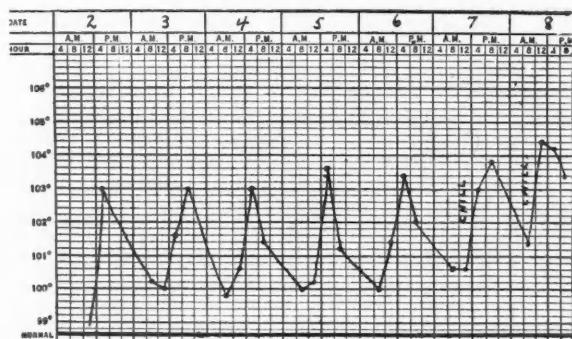


CHART 1. Case 1.—Remittent fever.

*Progress.*—Fever of the intermittent type continued, ranging from 100 to 104°. He had chills, lasting, on the average, about one-half hour.

Examination of his fundi, by Dr. F. T. Tooke, on November 21st was as follows: "The right eye shows a very well marked flame-shaped haemorrhage running obliquely from the lower disc margin down to the

temporal side. It is about the length of a disc diameter, and is associated with the wall of one of the venous capillaries. It is relatively recent. Both fundi are normal in all other respects."

On November 27th morphological blood examination (abbreviated) by Dr. J. Kaufmann was as follows. "Red blood cells 3,200,000; white blood cells 26,000; haemoglobin 54 per cent; colour index, 0.84. The blood picture shows a quite marked anaemia due to reduction in the red cell count and lowering in the haemoglobin concentration. The fragility of the erythrocytes is moderately increased, and this, with moderate bilirubinæmia, indicates that haemolytic factors are probably playing a rôle in the production of the anaemia. The sedimentation velocity is markedly increased. The white cells show a marked leucocytosis, due to an increase in polymorphonuclears, with decrease in nuclear segmentation and toxic changes in their cytoplasm. Eosinophiles are absent and the monocytes and lymphocytes show a relative and absolute reduction. This picture is that met with at the height of infection. The platelets are moderately reduced and there is considerable hydramia."

The patient's condition continued with daily chills and fever. At no time was enlargement of the spleen noted or petechiae observed. The diastolic murmur became somewhat more intense at the base. On November 28th, he became very dyspnoëic, which symptom increased in severity until his death the following day, November 29, 1933, twenty-seven days after his admission to the hospital and approximately six weeks after the onset of his cardiac condition. A diagnosis was made of gonococcal septicæmia and acute gonococcal aortic endocarditis.

*Autopsy.*—Permission for autopsy on the heart only was obtained. A section was also obtained from the spleen.

*Heart.*—Weight 370 grm. There were petechial hemorrhages on the posterior surface of the left ventricle. On the pericardium there was an area of petechial haemorrhages, about 3 cm. in diameter, over the posterior part of the base of the left ventricle. There were a few similar patches over the apex of the right ventricle. These were confined to visceral pericardium. The myocardium was pale reddish-brown. The left ventricle was moderately dilated, 1 cm. thick and uniformly firm. The papillary muscles were of normal size, pale grey, with mottled reddish areas. Chordæ tendineæ were slightly thickened and shortened; aortic valve, 5 cm. Involving the coronary free cusp there was a large polypoid mass which almost completely replaced it. This was 3 cm. long and extended into the cavity of the left ventricle. It was firm, dark and pale grey. There was extensive ulceration extending down from the free margin of the cusp to involve the undefended space. This was about 2 cm. in diameter. The polypoid mass filled the ulcerated area, extending through to the adjacent tricuspid valve on the right side, and was round and elevated, 2.5 cm. in diameter, and about 1 cm. above the endocardial surface. At the level of the tricuspid there was a small pale grey polypoid mass the size of a pea attached to the right coronary cusp of the aortic valve in the position of the corpora Arantii. The left coronary cusp was free and well preserved. Mitral valve, 8 cm. There was slight uniform thickening of the endocardium of the left auricle. Tricuspid, 10 cm.; pulmonary, 5 cm.

*Microscopic examination.*—Sections from the vegetation from the aortic valve showed masses of fibrinous material which were slightly laminated. At the periphery there were areas of leucocytes. Gram stain showed scattered Gram-negative diplococci. In some places these were intracellular, but in most areas no definite organisms were found. Diagnosis.—Fibrinous endocarditis (gonococcal).

*Myocardium.*—There were a few small foci of leucocytes. The muscle fibres in these areas were degenerating. There were no thrombosed vessels. Diagnosis.—Focal exudative myocarditis.

*Spleen.*—The pulp contained numerous plasma cells and large mononuclears. There was slight proliferation of the reticulum.

#### CASE 2

A female, married, aged 32, housewife.

*Complaints.*—Pain, redness and swelling of the right wrist and both ankle joints. Pain in both knees; chills and fever.

*History of illness.*—The patient had been perfectly well until eleven days before admission, at which time she had just returned from a vacation. After carrying her bag through the station she noticed on returning home that the right wrist was swollen and acutely painful. The following day, September 4, the right ankle became swollen and acutely painful, and she was forced to remain in bed. The following day, the left ankle became swollen, though the wrist was somewhat improved. Since the onset of the condition she had had frequent chills and had continued to run a fever. She was admitted to hospital on September 14, 1933.

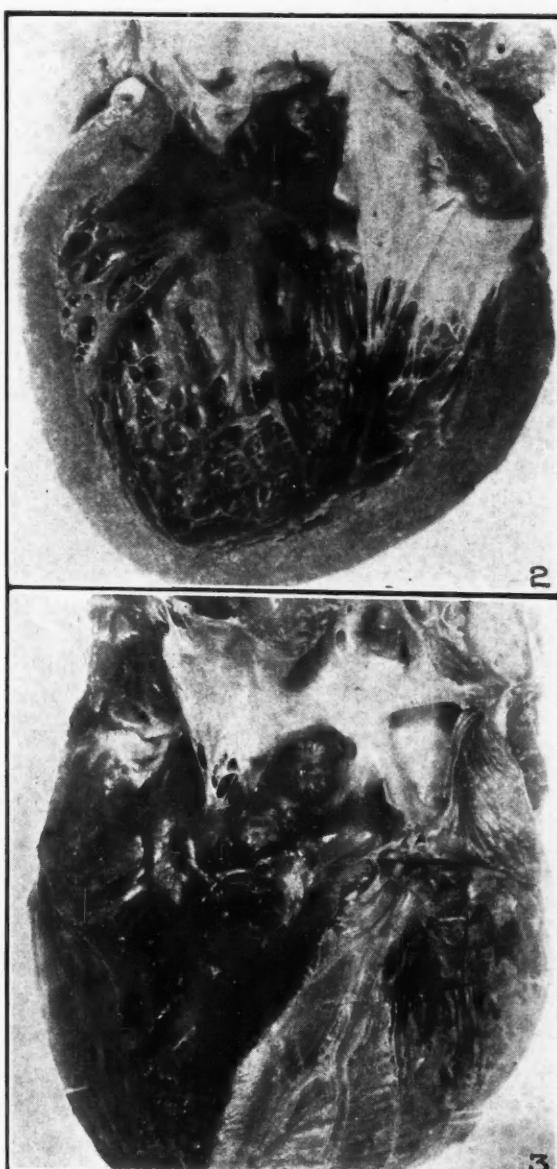


FIG. 2. Case 1.—Endocarditis and ulceration involving aortic valve and undefended space.

FIG. 3. Case 1.—Right side of heart showing ulceration extending through the septum to the tricuspid valve.

*Family history.*—Irrelevant.

*Personal history.*—There was no previous history of rheumatic fever or of heart disease.

*Physical examination* on admission revealed a temperature of 102°. The respirations were shallow, rapid, 42 per minute. She was in acute distress, perspiring freely, with large drops of perspiration on the skin. There was extreme pain, with swelling and redness of both ankle joints and the small joints of the right hand. There was swelling, though very little redness, of the left knee joint, together with evidence of free fluid in the joint. On the ventral surface of the index finger of the right hand was a dark reddened area, about 1 cm. in diameter, surrounding which was a border containing pus. It was considered embolic in origin. The whole finger was swollen and reddened. She was somewhat confused and spoke incoherently.

The pulse was regular, of good volume; no evidence of arterial thickening. Blood pressure was 135/65. The heart was not enlarged. A soft systolic murmur was present at the apex. The aortic second sound was clear. The lungs were clear. The spleen was not enlarged.

Pelvic examination revealed the urethra inflamed. A thin, purulent fluid exuded from Skene's tubules. The vaginal secretion was also purulent. The cervix showed marked bilateral lacerations and was eroded. The uterus was small, retroverted and fixed. There was slight thickening in both appendages, but no tenderness. There were no other palpable masses. The opinion was that it was a pelvic inflammation of a chronic nature.

*Laboratory examination.*—Urinalysis.—The urine had a specific gravity of 1028. Neither albumin nor sugar was present. Microscopic examination revealed scattered white blood cells and occasional granular casts.

Hæmatological examination (by Dr. J. Kauffmann).—Red blood cells 2,850,000; white blood cells 30,300; haemoglobin 44 per cent; colour index 0.78. The red blood cells were pale; slight alteration in sizes and shapes, good rouleaux; no crenation. There was a marked hypochromic anaemia, with evidences of regeneration and degeneration; hyperleucocytosis and neutrophilia and deviation of polymorphonuclears towards immature forms, accelerated sedimentation velocity, lymphocytopenia and monocytosis. There was evidence of a marked infective process with marked myeloid hyperactivity and little reparative effort.

The blood Wassermann test was negative; gonococcal fixation, 4 plus.

Blood culture.—Gonococci were isolated. A smear from the urethra showed no Gram-negative diplococci.

The electrocardiogram showed no preponderance; regular rhythm; rate 120 per minute. Normal auriculoventricular conduction time. There was slight depression of the S-T interval in leads I and II.

*Progress.*—She continued with frequent chills, and on the fifth day in the hospital suffered a severe one and her temperature rose to 107°. Fever of the remittent type continued, with daily flights as high as 105°.

On September 14th, the infected index finger was incised and a considerable amount of pus evacuated. On September 22nd, large petechiae appeared on the nail bed of the fingers and also on the conjunctiva. Examination of the heart now showed slight enlargement to the left. The systolic murmur at the apex had increased in intensity, and there was some roughen-

ing. Later in the day, petechiae appeared on the tip of the tongue. On September 25th, the blood pressure was 98/40. A blood transfusion of 500 c.c. was given. The following day the left knee joint was aspirated and 9 c.c. of fluid withdrawn. Culture of this fluid revealed no growth. On September 28th, the patient complained of precordial pain. On examination, a friction rub was present. There was definite cyanosis of the fingers and edema of the left leg. On September 29th, a second blood transfusion of 500 c.c. was given, and a third one on October 4th. On October 9th, microscopic blood appeared in the urine. She continued in this condition, at times irrational, and died on October 12th, forty days after onset of her illness. A diagnosis was made of gonococcal septicæmia, endocarditis and arthritis.

No autopsy was obtained.

Of interest in Case 1 is the presence of only slight cardiac hypertrophy (370 grm.) with a high degree of aortic insufficiency, attesting to the malignancy of the condition. In the presence of aortic insufficiency and without mitral stenosis, the mitral diastolic murmur heard at the apex was functional in origin and was a typical Austin Flint murmur. The ulceration extended through to the tricuspid valve on the right, involving the undivided space. That the bundle of His was involved was suggested from the electrocardiogram. Almost identical ulceration is present in a specimen in the McGill Medical Museum. This latter case was one of gonococcal endocarditis, clinically, but bacteriological studies were not available.

#### TREATMENT

Repeated small transfusions have been advocated, and in a case reported by Perry<sup>4</sup> with positive blood culture, endocarditis and emboli, recovery ensued. Recovery has also been reported in other instances, but in the majority of cases treatment has been unsuccessful. Gonococcus vaccine, antigenococcic serum, intravenous silver preparations, mercurochrome, and intravenous metaphen have been suggested, without beneficial results and often with severe reactions.

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## BENIGN EPITHELIAL INVASION\*

BY WILLIAM BOYD, M.D., F.R.C.P.(LOND.),

*Winnipeg*

INVASION of the deeper tissues by surface epithelium is one of the most easily recognized and significant of the evidences of malignancy. But such invasion is not necessary for a diagnosis of malignancy, and, on the other hand, it in itself is not necessarily malignant.

The columnar cells lining a tubular gland or covering a glandular surface may proliferate and form new glandular structures, not only on the surface but also in the depths of the tissue, to such an extent that the new formation may be widely separated from the original surface, although connected with it by a narrow tract. Should the latter be tortuous, the original connection with the surface can no longer be recognized in a single section, and a mistaken diagnosis of carcinoma may be made. Such a condition may be called benign epithelial invasion. Stratified epithelium is also liable to this change, as may be seen at the edge of a chronic ulcer of the skin or in the lining of the ureter. The columnar epithelium lining the gall bladder, Fallopian tubes, uterus and stomach offers excellent examples of the process.

It is in the *gall bladder* that the condition is seen in its most striking form and is most readily studied. In a perfectly normal gall bladder, although the mucosa is thrown into folds, the epithelium does not dip down into the underlying fibromuscular layer. But in many gall bladders removed surgically there is proliferation of the epithelium and invasion of the wall to form crypts. This condition, to which the descriptive name of *cholecystitis glandularis proliferans* has been applied by King and MacCallum,<sup>3</sup> of Melbourne, is present in about 10 per cent of such gall bladders. There is often a thickening of the wall over the area of epithelial proliferation, the most common site of which is at the fundus of the organ. These formations have been recognized for nearly 100 years, for Rokitansky noted mucosal outpouchings in 1842, and Aschoff called attention to their importance in 1905, so that they

are sometimes spoken of as the Rokitansky-Aschoff sinuses. They have also been called Luschka sinuses, but they must not be confused with the Luschka ducts ("true Luschka ducts" of Halpert<sup>1</sup>), to which they bear no relation. The latter are aberrant bile ducts which occur on the peritoneal surface, generally on the hepatic surface of the gall bladder. These have no connection with the mucosal surface, as can be shown by means of serial sections. Many observers have sought to trace a connection between the out-pouchings and increased pressure within the gall bladder, with the idea that they are pressure effects in the nature of herniations of the mucosa through the muscularis, which is not a continuous structure in the gall bladder (Fig. 1). From my own observations it appears much more probable that the process is an epithelial proliferation, the result of chronic irritation. Active chronic inflammation or indications of former inflammation can always be found, but there is usually no evidence of biliary obstruction which might cause an increase of pressure within the gall bladder.

These formations have been interpreted by some observers as pre-cancerous in character. There is no good reason for this view. Slade,<sup>4</sup> in a paper published in 1905, stated that early carcinoma of the gall bladder was present in 56 per cent of all cases of gall stones causing symptoms. Examination of his pictures shows that the condition was not early carcinoma but *cholecystitis glandularis proliferans*.

The neck which connects the deeper part of the pouch with the surface may be very narrow and is often tortuous (Fig. 2), so that the fundus of the pouch may appear to be completely isolated in the deeper tissues. It may become considerably dilated, giving a cystic appearance, and there may be a collection of these cysts quite close to the serosa, so that the thickened wall may appear to be honeycombed with ducts. The process may proceed to such an extent that a kind of diverticulum may be formed in which concretions are deposited, so that the observer may be misled into believing

\* Read at meeting of the Surgeons' Club, Winnipeg, on November 16, 1933.

that a calculus has ulcerated through the wall. The epithelium of these new glands may differ considerably from that which lines the surface, being tall and columnar in type, with clear mucin-filled cytoplasm and nuclei situated at the base of the cell. These cells may be regarded as intestinal in type, but as the gall bladder is derived from the epithelium of the primitive alimentary canal, such a change need occasion no surprise. It is sometimes difficult to draw a sharp line between this epithelial proliferation and neoplasia. The proliferated epithelium may be piled up on the surface and form a papillomatous mass instead of invading the deeper tissues.

The benign epithelial invasion may in rare cases take on the character of a true infiltrative neoplasm, as in a case studied in my laboratory

and recently reported by Wiglesworth<sup>5</sup> in this *Journal*. The patient, a woman 79 years of age, for ten years had a painless lump in the gall bladder region, which increased rapidly in size during the last six months till it formed a mass in the abdominal wall which extended from the costal margin to the crest of the ilium. At operation, the mass, which was continuous with the fundus of the gall bladder, was found to consist of a number of cysts. Microscopically, the wall of the gall bladder and the tumour with which it was continuous showed a picture of marked epithelial invasion with gland-formation (Fig. 3). Although it was not possible to be certain if the change in any given part was malignant, it is evident that the pathological process in the wall of the gall bladder and in

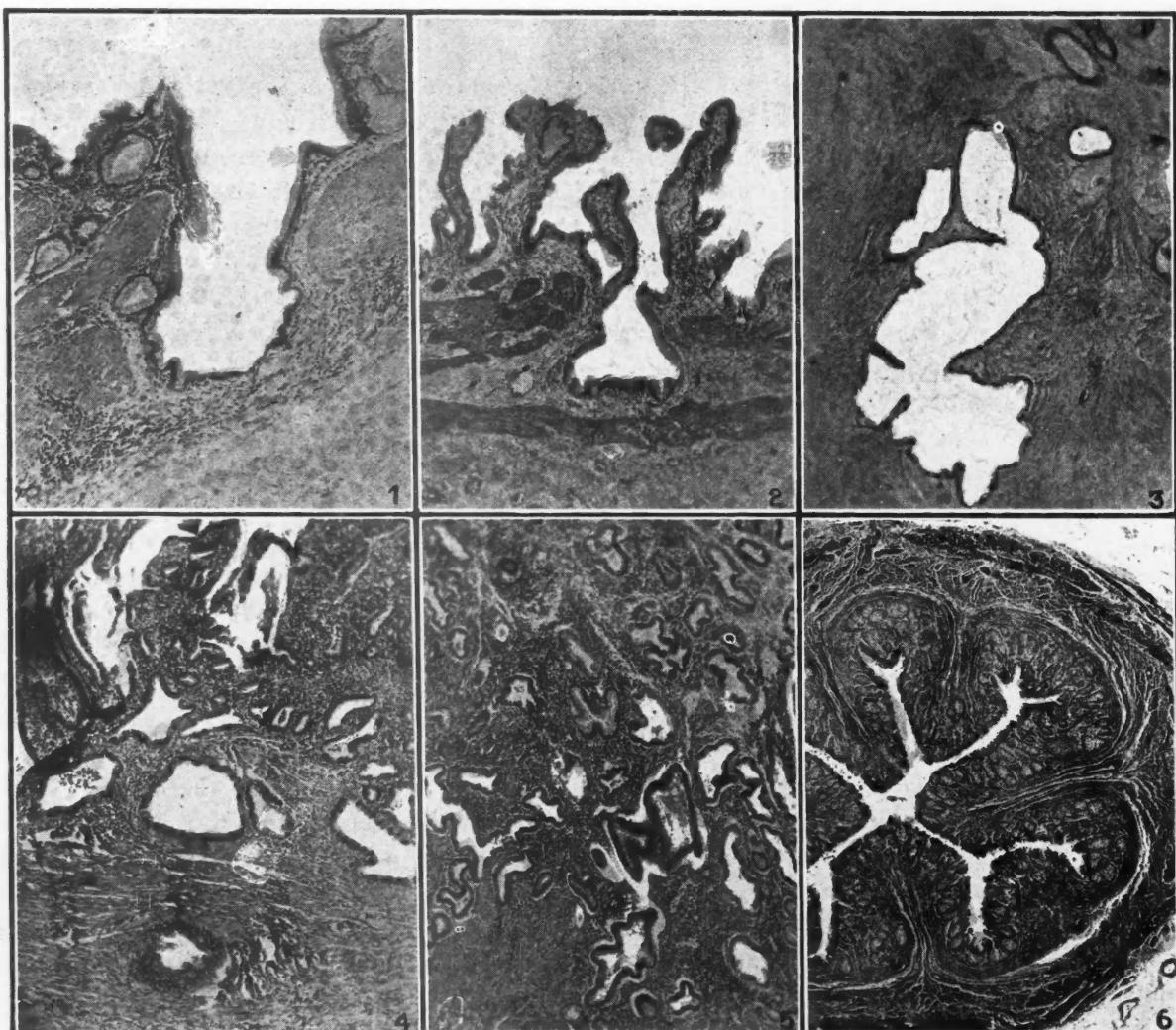


FIG. 1.—Out-pouching of mucosa through fibromuscular coat of the gall bladder, which might suggest the idea that it was caused by increased pressure.  $\times 75$ .

FIG. 2.—Showing characteristically narrow neck and penetration of fibromuscular coat. In other sections the appearance was that of a gland entirely separated from the surface.  $\times 35$ .

FIG. 3.—New epithelial formation in tissue between gall bladder and anterior abdominal wall.  $\times 50$ .

FIG. 4.—Benign epithelial invasion in Fallopian tube.  $\times 50$ .

FIG. 5.—Benign epithelial invasion in uterus.  $\times 50$ .

FIG. 6.—Benign epithelial invasion in the ureter. (From a specimen of Dr. Shields Warren).

the tumour of the abdominal wall was one and the same. The clinical course and the evidence of widespread invasion justify the assumption that we are observing the transition of a benign into a malignant process.

The process of benign epithelial invasion can be observed in other hollow muscular organs. The *Fallopian tube* offers one of the best examples. In chronic salpingitis a remarkable nodular thickening may sometimes be observed. This is caused by proliferation of the mucosal epithelium with a development of new glandular spaces in the depth of the wall, so that adenomatous masses may be formed deep down in the muscularis. The usual explanation given is that the epithelial cells of the mucosa, or perhaps portions of the entire mucosa, are squeezed by intratubal pressure into the substance of the muscular wall, where they produce true follicles, but there can be no doubt that there is an actual proliferation of epithelium and a formation of new glandular spaces. As this always appears to be associated with the presence of chronic inflammation, it is reasonable to suppose that the epithelial overgrowth is the result of long-continued irritation.

The *uterus* may also be the site of benign epithelial invasion. The line of division between endometrium and muscularis, which is never very sharp in this organ, is lost in endometrial hyperplasia, the condition which used to be known as glandular endometritis, and which appears to be due to over-production of oestrin and absence of corpus luteum activity. In such cases the glands of the endometrium may penetrate into the muscular wall for a considerable distance, owing to proliferation of the lining epithelium (Fig. 5). In adenomyoma of the uterus, which may be regarded as an exaggeration of this condition, the endometrium invades the muscularis, sometimes as far as the serous coat.

The *stomach* sometimes provides examples of the condition under discussion. In chronic gastritis or at the edge of a chronic ulcer there may be an atypical epithelial proliferation, with formation of new glands which penetrate between the bundles of the muscularis mucose and reach the submucosa, a state of affairs which may

be mistaken for carcinoma. Hurst and Stewart<sup>2</sup> found this epithelial heterotopia in 22 per cent of cases of chronic ulcer and in 40 per cent of cases where the ulcer had undergone complete cicatrization. In my own material these new formations have been much less striking than those which are found in the gall bladder, Fallopian tube and uterus.

It is difficult to say to what extent these examples may be multiplied. The epithelial downgrowth which occurs at the edge of an indolent ulcer of the skin and which may be so invasive as easily to be mistaken for malignancy is so familiar that it needs only to be mentioned. It is possible that the rupture which occasionally results from obliteration of the proximal end of the appendix and the formation of a mucocele, and which may be followed by the development of pseudomyxoma peritonei should be ascribed to epithelial invasion of the wall. In a section of the ureter which Dr. Shields Warren kindly sent me there was a most remarkable degree of benign epithelial invasion involving the entire circumference of the tube (Fig. 6).

The conception of benign epithelial invasion appears to be a useful one. Individual examples in such organs as the gall bladder, tube, uterus, stomach, and skin have long been recognized, but the mere act of grouping them together serves to call attention to a process which can be looked for in other organs. To the surgical pathologist a recognition of this possibility is of especial importance.

#### SUMMARY

Invasion of the deeper tissues by surface epithelium, whilst a hall mark of malignant disease, may also occur in benign conditions. Some of the more striking examples of this process have been collected under a common heading, but others can doubtless be added to the list.

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## ONE THOUSAND AVERTIN ANÆSTHESIAS

BY WESLEY BOURNE, M.Sc., M.D., C.M., F.R.C.P.(C.) AND  
P. E. O'SHAUGHNESSY, M.D., C.M.,

*Montreal*

ALTHOUGH the literature on avertin is extensive, the use of this anæsthetic is not yet universal. It is therefore relevant to analyze collected clinical data. One thousand administrations of avertin are accordingly reported.

Several important actions of avertin have been described: how it obtunds the nervous system<sup>1, 2</sup> (this is the desired therapeutic effect); how respiration<sup>2</sup> is depressed; how the circulation<sup>3</sup> is influenced; how the blood<sup>4</sup> becomes concentrated and less alkaline; and how the functions of the liver<sup>4, 5, 6</sup> and kidneys<sup>4</sup> are somewhat impaired. The clinical and laboratory investigations on these actions have shown that avertin, in comparison with other anæsthetics, may be considered practically safe and

without contraindication, provided suitable doses are used. So true is this that it seems timely to predict an abiding usefulness for avertin. Its employment is on the increase.

Table I sets forth the various doses employed, as well as the numbers and percentages of the cases in this series. It will be seen that the doses range from 70 to 150 mg. per kilo. of body weight. In the earlier cases the standard dose from which we worked was 100 mg. per kilo. Later it was decided to raise this to 125 mg. per kilo. It is evident that in all of the cases nearly 34 per cent did not require any other general anæsthetic than the avertin given, whereas, when the doses were around 100 mg. per kilo. (90, 100 and 110), only 25 per cent

TABLE I.  
AVERTIN: DOSES AND NUMBERS OF CASES

Doses: mg. per kg.	Total Number of Cases	Without other General Anæsthetics				With Nitrous Oxide				With Nitrous Oxide and Ether				With Ether				With Chloroform	
		Avertin alone	With Procaine	With Cocaine	With Pernafeine	With Nitrous Oxide only	With Procaine	Totals and Percentages	With Nitrous Oxide and Ether	With Procaine	Totals and Percentages	With Ether only	With Procaine	Totals and Percentages	With Ether	Percentages			
70	1	1																	
80	20	3	1			5	2		6	2			1						
90	12	3	1	1		3	1		3										
100	474	61 (12.9%)	43	11		134 in 534 = 25.1%	159 (33.5%)	20	194 in 534 = 36.3%	120 (25.3%)	11	151 in 534 = 28.3%	32 (6.7%)	2	36 in 534 = 6.7%	15			
110	48	10	3	1		10	1		14	3		2		4	3.5%				
115	17	11	1			2			3										
120	42	10	5	2		192 in 435 = 44.1%	13		168 in 435 = 38.6%	3	5				11 in 435 = 2.5%	1			
125	360	133 36.9%	12	9		435 (38.9%)	140	8	435 (12.5%)	45		58 in 435 = 13.3%	3		8 (2.2%)	5	1.4%		
135	16	9				4	1		2										
150	10	6				2			2										
1000	247	66	22	2	(337)	338	33	(371)	198	21	(219)	46	2	(48)	25				

could be similarly managed, as against 44 per cent when the doses were in the neighbourhood of 125 mg. per kilo. (115, 120, 125 and 135); that in all of the cases about 25 per cent had avertin only, whereas for the smaller standard dose the percentage is only 13 as against 37 in the event of the larger quantity; and that 37 per cent of all cases received nitrous oxide as the only other general anaesthetic, while the differences between the percentages of the cases of the smaller and larger doses are not so marked; also, that the remaining 29 per cent of the cases were given nitrous oxide and ether, ether alone, or chloroform as supplementary anaesthetics, the percentages in each instance being considerably greater when doses of avertin were smaller than when they were larger, as one would naturally expect.

When regional anaesthesia is combined with the use of avertin, there is no doubt that this practice lessens the necessity of additional general anaesthetics, afferent impulses being diminished. We regret that this procedure was not

adopted more often, although it has been highly commended elsewhere.<sup>7</sup>

Let us now consider those cases in which the smaller doses were given. One woman of ninety years of age received 70 mg. of avertin per kilo. of body weight. She was suffering from a fracture-dislocation of the hip. Anaesthesia was complete and she recovered without complications.

There were 20 cases in which 80 mg. per kilo. were given. The reasons for this small dose are not far to seek; they are set forth in Table II. The ages were from 27 to 76, most of them nearer the latter, which in itself was a factor determining the size of the dose, the belief being that elderly people should have relatively small quantities. Three subjects aged 27, 35 and 45 had lost weight, and this was the reason for the reduced doses; on all three laparotomies were performed; two required nitrous oxide only in addition, and one a little ether as well. Two were immoderately obese. On one of these colporrhaphy was done and no other anaesthetic

TABLE II.  
CASES OF EIGHTY MILLIGRAMS PER KILOGRAM

No.	Age	Sex	Other Anæsthetics	Operation	Condition	Remarks
1	52	M.	Procaine $N_2O$ and $Et_2O$	Cholecystectomy		No nausea. Appendix removed.
2	54	M.	$N_2O$ and $Et_2O$	Cholecystectomy	Deeply jaundiced	No nausea
3	48	F.	$N_2O$ and $Et_2O$	Cholecystectomy		Vomited bile few times.
4	44	M.	$N_2O$ and $Et_2O$	Cholecystectomy	Very obese	Appendix removed.
5	67	F.	$N_2O$ and $Et_2O$	Cholecystostomy	Gall stones	Vomited bile twice.
					Fat necrosis	Died in 29 hours.
6	66	F.	$N_2O$	Cholecystostomy	Acute pancreatitis	(No. 6, Table IX)—pulmonary collapse.
7	47	F.	$N_2O$ and $Et_2O$	Hysterectomy	Anæmia	Vomited bile. Operation 39 days later (No. 8, Table III).
8	76	M.	$N_2O$ and $Et_2O$	Anterior gastro-enterostomy	Carcinoma of stomach	No nausea.
					Very anæmic	Died 30 hours later. Gastric hemorrhage (No. 7, Table IX).
9	35	M.	Procaine $N_2O$ and $Et_2O$	Appendicectomy	Loss of weight	Vomited once.
10	76	M.	Ether	Proctoscopic examination		No nausea.
11	27	F.	$N_2O$	Bilateral salpingo-ophorectomy	Loss of weight	Slight nausea.
12	63	M.	Procaine $N_2O$	Appendicectomy		Appendix removed.
13	72	F.	Procaine $N_2O$	Mammectomy	Carcinoma	No nausea.
14	72	F.	$N_2O$	Mammectomy		No nausea.
15	73	F.	$N_2O$	Mammectomy	Carcinoma	No nausea.
16	45	M.	$N_2O$	Exploratory laparotomy	Loss of weight	Vomited once. Appendix removed.
17	60	F.	Procaine	Exploratory laparotomy		No nausea. Appendix removed.
18	50	F.	None	Anterior and posterior colporrhaphy	Very Obese	Vomited once.
19	34	F.	None	Implantation of radium—uterus		No nausea.
20	42	F.	None	Curettage	Anæmic	No nausea.

TABLE III.  
CASES OF NINETY MILLIGRAMS PER KILOGRAM

No.	Age	Sex	Other Anæsthetics	Operation	Condition	Remarks
1	54	F.	N <sub>2</sub> O and Et <sub>2</sub> O	Cholecystectomy		Vomited once. Appendix removed.
2	44	F.	N <sub>2</sub> O and Et <sub>2</sub> O	Oophorectomy	Large cyst	No nausea.
3	8	M.	N <sub>2</sub> O and Et <sub>2</sub> O	Mastoideectomy		Vomited a few times.
4	57	F.	Procaine N <sub>2</sub> O	Exploratory laparotomy	Hæmorrhage	Died 5 days later (No. 8, Table IX).
5	55	F.	N <sub>2</sub> O	Hysterectomy	Cachectic carcinoma	No nausea.
6	60	F.	N <sub>2</sub> O	Excision of lipoma		Slight nausea.
7	70	F.	N <sub>2</sub> O	Mammectomy	Carcinoma	No nausea.
8	66	F.	Procaine	Exploratory laparotomy Drain—lesser cavity.	Pancreatitis	Died in 3 days; operation 39 days before. (No. 11, Table IX).
9	69	M.	Cocaine	Iridectomy	Acute glaucoma	No nausea.
10	51	F.	None	Reduction—Pott's fracture	Obese	No nausea.
11	68	F.	None	Closed reduction—fractured hip		No nausea.
12	88	F.	None	Closed reduction—fractured hip		No nausea.

was necessary; the other, a case of cholecystectomy, was given nitrous oxide with some ether. Of the three cases complicated with anaemia, one had a hysterectomy done; she required ether as well as nitrous oxide. The second, a case of carcinoma of the stomach, had to have some ether with the nitrous oxide. The third, in which the operation was curettage of the uterus, did not need supplemental anaesthesia. There were 6 gall-bladder cases, in 2 of which cholecystostomy was performed, and in 4, cholecystectomy. In all of these six, additional anaesthesia was necessary. The remaining cases are sufficiently explained in the Table. In all but 4 of the 20 cases, other general anaesthetics

had to be used, and it is evident that larger doses of avertin might have been given with safety.

Table III supplies the data concerning those occasions when 90 milligrams of avertin per kilo. of body weight were administered. The particulars of this group of cases are similar to those of Table II, with the exception that they seemed to warrant a larger dose.

Attention may now be turned to the other extreme in doses employed. On sixteen occasions, 135 mg. of avertin per kilo. of body weight were given (Table IV). The majority of the patients in this group were young, or very strong, or both. There was one case of

TABLE IV.  
CASES OF ONE HUNDRED AND THIRTY-FIVE MILLIGRAMS PER KILOGRAM

No.	Age	Sex	Other Anæsthetics	Operation	Remarks
1	38	F.	None	Herniorrhaphy—inguinal	No nausea
2	4	M.	None	Suturing soft palate	No nausea
3	16	M.	None	Appendicectomy	No nausea
4	8	M.	None	Mastoideectomy	No nausea
5	12	M.	None	Reduction of dislocated elbow	No nausea
6	16	F.	None	Tonsillectomy	No nausea. Oxygen intra-tracheally
7	6	F.	None	Tonsillectomy	No nausea
8	19	M.	None	Open reduction—fractured olecranon	No nausea
9	17	M.	None	Plastic—lip. Extraction—2 teeth	No nausea. Old cleft-palate case
10	10	M.	N <sub>2</sub> O	Appendicectomy	No nausea
11	33	F.	N <sub>2</sub> O	Removal of polyp of cervix uteri	Moderate nausea
12	37	M.	N <sub>2</sub> O	Excision of head of radius	No nausea
13	52	F.	N <sub>2</sub> O	Removal of carcinoma of face	No nausea. Intratracheal.
14	52	M.	Procaine N <sub>2</sub> O	Thyroidectomy	No nausea. Exophthalmic goitre
15	14	M.	N <sub>2</sub> O and Et <sub>2</sub> O	Herniorrhaphy and appendicectomy	Slight nausea
16	18	M.	N <sub>2</sub> O and Et <sub>2</sub> O	Tonsillectomy	No nausea. Pharyngeal.

TABLE V.  
CASES OF ONE HUNDRED AND FIFTY MILLIGRAMS PER KILOGRAM

No.	Age	Sex	Other Anæsthetics	Operation	Remarks
1	3/4	F.	None	Secondary suturing—abdomen	Wt. 10 kg. Died 4 days after from pneumonia. Suffering pneumonia after operation for intussusception 10 days previously (No. 5, Tab. IX)
2	42	M.	None	Iridectomy, right	No nausea (Same case. Previously had had cocaine for nasal operation and showed marked systemic reaction.)
3	42	M.	None	Iridectomy, left	No nausea
4	32	M.	None	Resection of nasal septum	No nausea. Oxygen intratracheally
5	16	M.	None	Appendicectomy	No nausea. Awakening effects successfully demonstrated by 1.5 gr. ephedrine intravenously (Ref. 8).
6	22	M.	None	Removal of plate-femur	No nausea.
7	6	F.	N <sub>2</sub> O	Removal of plate-ulna	Vomited several times. Acetone on breath, marked. Did not have phosphate rectal solution (Ref. 9).
8	6	M.	N <sub>2</sub> O	Appendicectomy	No nausea
9	13	M.	N <sub>2</sub> O and Et <sub>2</sub> O	Appendicectomy	No nausea
10	8	F.	N <sub>2</sub> O and Et <sub>2</sub> O	Tonsillectomy	No nausea. Pharyngeal.

TABLE VI.  
AVERTIN WITHOUT OTHER GENERAL ANÆSTHETICS

Operation	No. of Cases	Milligrams per Kilogram											No. with Local	Remarks
		70	80	90	100	110	115	120	125	135	150			
Appendicectomy.....	58				16	2	1	4	33	1	1	25Pr.	Procaine infiltration	
Cholecystectomy.....	2				2							2Pr.	1 spinal; 1 com. duct drain	
Gastro-enterostomy.....	1				1							1Pr.		
Hysterectomy.....	10					2	2		6			2	appendicectomy	
Exploratory laparotomy..	12		1		5	1	1		4			4Pr.	8 app.; 2 öoph.; 2 adhesions	
Salpingo-öophorectomy..	5								5			4	appendicectomy	
Miscellaneous abdominal..	3			1	1						1	2Pr.	Nos. 5 and 11, Table IX; other, replacing coecostomy	
Herniorrhaphy.....	19					7		1	9	1		5Pr.	All inguinal. 2 bilateral, 3 spinal, 3 appendicectomy	
Antrum.....	6					1		1	4			2Np.	4 radical, 2 intranasal, 4 oxygen intratracheally	
Mastoid.....	2								1	1		1	bilateral	
Nasal septum.....	6								5			6Ce.	3 turbinectomy	
Tonsillectomy.....	13				4				7	2		10	oxygen intratracheally	
Cataract.....	4				2				2			4Ce.	Cocaine instillation	
Enucleation, eye.....	3				1				2			3Ce.	Cocaine instillation	
Iridectomy.....	10			1	6				1		2	8Ce.	2 of 150 mg. Same case without Ce—previous reaction	
Miscellaneous, eye.....	3				2				1			2Ce.	2 plastic; 1 removal of tear sac	
Dental.....	26					3	4	6	11	2				
Dressings and skin grafts..	28			1	12	3			13			2Pr.	5 skin graftings	
Fractures and dislocations.	42		3	14		1	1	19	2	1		3Pr.	1 spinal	
Gynaecol., minor.....	20			8	1			8				2Pr.	2 sacral anæs. for "general repair"	
Mammectomy.....	12				6		2		4			1Pr.	6 radical	
Thyroidectomy.....	5				3				2			5Pr.	3 toxic	
Thoracotomy.....	6				6							6Pr.		
Urological.....	10				4	2			4			3Pr.	Kidney 2, bladder 2, cystostomy 2, hydrocele 2, orchidectomy and circumcision	
Miscellaneous.....	31				14			4	13			4Pr.	Decompression 2, cesophagoscopy 2, and various minor operations	
		337	1	4	5	115	14	12	17	154	9	6	90	14 intratracheal

Pr. = Procaine, Np = Nupercaine, Ce. = Cocaine.

toxic goitre in which it was necessary to give nitrous oxide in spite of the fact that procaine had been used. It will be noticed that in more than one-half of the cases avertin was the only anaesthetic used. Anaesthesia was complete in each of these instances.

The ten cases in which 150 mg. per kilo. were employed (Table V) were also young or youngish patients, similar to those of the preceding Table. In six instances no other anaesthetic was needed. In spite of the relatively large doses used in the cases set forth in Tables IV and V, inhalation anaesthetics had to be used fairly often, and on four occasions it was necessary to add small quantities of ether. It is pointed out, however, that when nitrous oxide is being administered after avertin has been given, oxygen may be used

more freely than otherwise, and that when it is necessary to add ether a very small quantity is sufficient. These two facts are all the more true for the larger doses in antithesis to the smaller doses of avertin. This is a strong argument in favour of the larger doses of avertin.

Several facts which have been posited in the foregoing Tables are confirmed in Tables VI, VII and VIII and, being evident, need no further comment. Attention is drawn to the variety of operations in each list. It is worthy of note that it was necessary to use other general anaesthetics for the so-called major operations more often than for others; this is especially true of operations on the upper abdomen. It is also worthy of note that the majority of these "major" cases were given smaller doses and

TABLE VII.  
AVERTIN WITH NITROUS OXIDE AS THE ONLY OTHER GENERAL ANAESTHETIC

Operation	No. of Cases	Milligrams per Kilogram										'No. with Procaine'	Remarks
		80	90	100	110	115	120	125	135	150			
Appendectomy.....	97	1		42	2	1	7	42	1	1	15		6 intratracheal; 1 appendectomy.
Cholecystectomy.....	10		9	1							4		1 of 80 mg. Died 39 days later after second operation (No. 11, Table IX).
Cholecystostomy.....	2	1		1									3 intratracheal; 1 part. gastrectomy; 1 anterior gastro-enterostomy; 1 with appendectomy.
Gastro-enterostomy.....	8			7				1					3 appendectomy; 1 oophorectomy.
Hysterectomy.....	15		1	2	1		2	9					18 appendectomy; 2 oophorectomy; 4 inoperable.
Exploratory laparotomy..	24	1	1	12	1						1		9 appendectomy; 3 vent-suspension.
Salpingo-oophorectomy...	14	1		7				6					1 Cæs. sec.; 4 vent.-suspension and app.; 1 volvulus; 1 adhesion; 1 res. cæcum.
Miscellaneous abdominal..	8			5			1	2					4 femoral; 9 bilateral inguinal; 2 ventral-postoperative.
Herniorrhaphy.....	48			25	4	1	1	17			5		8 radical; 4 bilateral; 1 intranasal; 7 intratracheal.
Antrum.....	9			2				7					1 intratracheal.
Mastoid.....	3			1				2					29 intratracheal; 16 pharyngeal.
Nasal septum.....	1							1					1 intratracheal; turbinectomy.
Tonsillectomy.....	45			10				35					16 radical.
Ethmoid.....	1							1					Both very toxic.
Skin grafting.....	3			1				2					Kidney 5, bladder 1, urethrotomy 1 (No. 25, Table IX).
Fractures and dislocations.	20			10	1			7	1	1	1		4 intratracheal—"Ca" face and neck, glands, lipomas, etc.
Gynaecol. minor.....	16			13				2	1				
Mammectomy.....	22	3	1	14	1		2	1			2		
Thyroidectomy.....	2			1				1			2		
Thoracotomy.....	4			3				1					
Urological.....	7			4				3			1		
Miscellaneous.....	12		1	10					1		2		
	371	7	4	179	11	2	13	148	5	2	33		51 intratracheal.

required additional anaesthesia; this is most strikingly true of cholecystectomies, cholecystostomies and exploratory laparotomies. These smaller doses were decided upon deliberately in accordance with earlier views—views which are still current. We have here another strong argument in favour of using larger doses of avertin than has been customary. In other words, one should endeavour to give so much avertin that ether will not be necessary, although a great deal of caution must be exercised in this direction. However, such an ideal has been partly attained, in that nitrous oxide alone was frequently sufficient as an anaesthetic additament and that when ether was used its quantity was relatively small.

The critical position into which one is brought by recommending larger doses as it accounts for, so it justifies, an explanation of what is meant by exercising caution concerning them. The amount of avertin per kilogram of body weight should be decided upon only after a careful evaluation of the patient by considering the following:—*Age*; the young stand avertin better than old people, just as the strong are more resistant than those who are weak. *Habits*; those who live active lives may have more avertin than those who are sedentary, just as those who indulge in alcohol or other drugs will be found to be more tolerant to it than those who do not. *Weight*; marked variations in either direction from standard values should indicate reduced doses.

TABLE VIII.

## AVERTIN WITH NITROUS OXIDE AND ETHER, WITH ETHER ALONE, AND WITH CHLOROFORM ALONE

Operation	No. of Cases	Milligrams per Kilogram										No. with Procaine	Remarks
		80	90	100	110	115	120	125	135	150			
Appendectomy.....	71	1	1	43		2	7	17		1	6	3 CHCl <sub>3</sub> , 14 Et <sub>2</sub> O alone.	
Cholecystectomy.....	28	4	1	18	2		1	2			3	16 intratracheal; 9 appendectomy.	
Cholecystostomy.....	6	1		5								3 intratracheal; 1 appendectomy.	
Gastro-enterostomy.....	10	1		5	1		2	1			1	3 intratracheal; 1 gastrectomy; 3 appendectomy.	
Hysterectomy.....	13	1		7	2	1		3				1 CHCl <sub>3</sub> , 3 Et <sub>2</sub> O alone.	
Exploratory laparotomy..	31			22	4	1		4			2	6 Et <sub>2</sub> O alone; 3 intratracheal. (See Legend No. 1, below.)	
Salpingo-öophorectomy...	8		1	3				4				2 Et <sub>2</sub> O alone; 3 appendectomy.	
Miscellaneous abdominal..	6			6								2 gastrectomy; 2 perf. duoden. ulcer; 2 abdominal abscess.	
Herniorrhaphy.....	34			17	7			9	1		2	1 CHCl <sub>3</sub> , 6 Et <sub>2</sub> O alone; 5 ventral, 3 bilateral, 3 appendectomy.	
Antrum.....	6							6				6 intratracheal, all radical; 2 bilateral and 1 tonsillectomy.	
Mastoid.....	2		1	1								2 Et <sub>2</sub> O alone.	
Nasal septum.....	3			3								1 CHCl <sub>3</sub> ; 2 intratracheal.	
Tonsillectomy.....	13			3				8	1	1		11 intratracheal; 2 pharyngeal.	
Eye.....	5			2		2	1					5 CHCl <sub>3</sub> ; 3 iridectomy; 2 plastic.	
Skin grafting.....	3			3								2 ether alone.	
Fractures and dislocations.	20			13	6			1			3	4 chloroform; 4 ether alone.	
Gynaecol. minor.....	6			5				1				1 CHCl <sub>3</sub> , 2 Et <sub>2</sub> O alone.	
Mammectomy.....	7			5	1			1				5 radical; 2 ether alone.	
Thoracotomy.....	1			1							1	1 CHCl <sub>3</sub> .	
Urological.....	5			5							2	2 Et <sub>2</sub> O; 1 circumcision; 1 orchidectomy; 2 lithotrity; 1 nephrectomy.	
Miscellaneous.....	14	1		13							3	3 ether alone; 2 intratracheal; 8 CHCl <sub>3</sub> . (See Legend No. 2 below.)	
	292	9	3	180	23	3	12	58	2	2	23	25 with chloroform; 48 with ether alone; 46 intratracheal.	

Legend No. 1—21 appendectomies, 2 cases of volvulus, 3 adhesions, 1 inoperable, 1 haemorrhagic pancreatitis, 1 partial gastrectomy, 1 pancreatic cyst and 1 biopsy of the omentum.

Legend No. 2—3 rectal, 2 lipomas, 1 subacromial bursa, 2 carcinoma of face, 1 cyst of neck, 1 foreign body of hand, etc.

*Physical condition;* cachectic, anaemic and wasted individuals, as a rule, may not have large doses of avertin, an exception being that those who suffer from exophthalmic goitre stand large doses of this drug very well. In short, one should find out as much as possible about the individual patient before deciding

on the amount of avertin to be given, and when the amount has been decided upon, it should then be instilled into the rectum very slowly (7 and 8); about ten minutes ought to be taken.

One hundred and nine operations were performed in the field of ear, nose and throat

TABLE IX.  
DEATHS AFTER ONE THOUSAND AVERTIN ANÆSTHESIAS

No.	Cause	Operation	Time after Operation	Sex	Age	Mg. per Kg.	Other Anæsthetics	Remarks
1	(2nd day) Pneumonia....	Cholecystectomy	77 hours	F.	68	100	N <sub>2</sub> O and Et <sub>2</sub> O Procaine	No autopsy. Mod. circulatory depression.
2	(next day) Pneumonia....	Cholecystectomy	48 hours	F.	45	100	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Myocarditis and miliary tuberculosis.
3	(16th day) Pneumonia....	Anterior gastro-enterostomy	18 days	M.	68	100	N <sub>2</sub> O	Autopsy. Advanced carcinoma. Mod. circulatory depression.
4	(3rd day) Pneumonia....	Gastrotomy, Gastro-enterostomy	7 days	F.	13	110	N <sub>2</sub> O and Et <sub>2</sub> O Procaine	Splenectomy 4 years ago. Operation now for haemorrhage from duodenal ulcer.
5	Pneumonia ...	Secondary suturing	4 days	F.	3/4	150	None	Operation 10 days before for intussusception (Table VI, No. 7 and Table V, No. 1) Autopsy.
6	Pulmonary collapse.....	Cholecystostomy	29 hours	F.	67	80	N <sub>2</sub> O and Et <sub>2</sub> O	Gall stones and fat necrosis (Table II, No. 5).
7	Hæmorrhage..	Anterior gastro-enterostomy	30 hours	M.	76	80	N <sub>2</sub> O and Et <sub>2</sub> O	Carcinoma. Very anaemic. (Table II, No. 8.)
8	Hæmorrhage..	Exploratory laparotomy	5 days	F.	57	90	Procaine N <sub>2</sub> O	Autopsy. Syphilitic. Hæmorrhage from eroded gastric artery (Table III, No. 4).
9	Hæmorrhage..	Partial gastrectomy	21 days	M.	46	100	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Marked circulatory depression.
10	Hæmorrhage..	Partial gastrectomy	4 hours	F.	66	100	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Carcinoma of stomach.
11	Pancreatitis...	Drainage of lesser cavity	72 hours	F.	66	90	Procaine	Autopsy. Cholecystostomy 39 days before (Table VI, No. 7 and Table III, No. 8).
12	Pancreatitis...	Exploratory laparotomy	72 hours	M.	30	125	Ether	Autopsy. Hæmorrhage in upper abdomen.
13	Hæmorrhage..	Cholecystectomy	5 days	M.	61	100	N <sub>2</sub> O and Et <sub>2</sub> O	Internal hæmorrhage.
14	Obstruction...	Exploratory laparotomy	48 hours	M.	33	125	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Carcinoma of liver. Volvulus.
15	Obstruction...	Coecostomy	8 hours	F.	53	110	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Miliary tuberculosis. Volvulus.
16	Obstruction...	Colostomy	76 hours	F.	32	100	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Carcinoma of sigmoid; adhesions, peritonitis and myocarditis.
17	Obstruction...	Salpingo-oophorectomy	48 hours	F.	29	125	N <sub>2</sub> O	Autopsy. Adhesions and peritonitis.
18	Peritonitis....	Cholecystectomy	19 days	F.	65	100	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Subdiaphragmatic abscess.
19	Peritonitis....	Appendectomy	11 hours	F.	38	115	N <sub>2</sub> O and Et <sub>2</sub> O	Gangrenous appendix; quantities of pus; very toxic beforehand.
20	Peritonitis....	Appendectomy	70 hours	M.	51	120	N <sub>2</sub> O and Et <sub>2</sub> O	Acute perforated appendix. Nephritis.
21	Carcinoma....	Exploratory laparotomy	19 days	M.	52	100	N <sub>2</sub> O and Et <sub>2</sub> O	Autopsy. Very advanced carcinoma of liver and tuberculosis of lungs.
22	Carcinoma....	Mammectomy	3 hours	F.	63	100	Procaine N <sub>2</sub> O	Very advanced carcinoma. Restless after, but did not regain consciousness.
23	Paget's disease	Partial removal of tumour	26 hours	F.	55	100	Procaine	Tumour, skull. Marked circulatory depression.
24	Fractured skull	Suturing hands and spinal puncture	14 hours	M.	50	100	None	Unconscious before and after.
25	Uræmia.....	Urethrotomy	6 days	M.	47	100	N <sub>2</sub> O	Carcinoma of penis.

surgery, in 27 of which avertin was the only anæsthetic employed, in 58 nitrous oxide was used with the avertin, and in 24 some ether had to be added to the nitrous oxide. On 71 occasions intratracheal insufflation was performed. Several times this was done even when avertin was the only anæsthetic employed, and then oxygen was blown into the trachea. Often when nitrous oxide was insufflated we might have done without it. The advantages of insufflation are now no longer in question. Although these series of operations do not contain many on the eye, yet, as has been affirmed elsewhere,<sup>10</sup> our ophthalmologist, Dr. A. Bramley Moore, expresses great satisfaction with avertin anaesthesia.

These three Tables (VI, VII and VIII) require no further explanation.

In this series of 1,000 cases, the occurrence of nausea and vomiting has been investigated in all. Even when these manifestations were very slight they were counted. We are fully aware of the variety of factors which influence their occurrence and are mindful of the difficulty of securing absolutely accurate notes concerning them, yet it has seemed worth while to record the results.

Nausea and vomiting after avertin	Percentage
alone .....	25 in 337 = 7.4
with N <sub>2</sub> O .....	67 in 371 = 18.0
with N <sub>2</sub> O + Et <sub>2</sub> O or	
Et <sub>2</sub> O alone .....	99 in 267 = 37.0
with CHCl <sub>3</sub> .....	3 in 25 = 12.0
194 in 1,000	= 19.4

We are quite sure that avertin by itself causes no nausea, just as we believe that it is the best anæsthetic extant for inducing peaceful sleep.

Before going on to the most sombre proposition of this work, that of considering the deaths, a short digression may be allowed. It is well known that the administration of avertin is followed by a long period of unconsciousness. It is granted that this feature has many advantages, among which one has recently come to our attention, namely, that a patient may be brought back to the operating room several times without his knowledge, for such incidents as post-operative haemorrhage or the resetting of fractures.

Of these 1,000 persons to whom avertin was given, 25 subsequently died. A perusal of Table IX will persuade one that avertin

can hardly be blamed for any of these deaths. It has been shown that avertin causes death primarily by depressing the respiratory centre.<sup>1, 2</sup> It has also been shown that respiratory depression is considerably lessened when avertin is administered slowly.<sup>7, 8</sup> In none of the 25 patients who died was respiration unusually depressed, so much so that it was not necessary to use respiratory stimulants. It will be seen that 21 of them had to have other general anæsthetics, and that 16 of these required ether, which points to the fact that the depression of avertin itself was not severe. Who can say, of the cases with pulmonary complications, how much influence there was attributable to avertin? We believe that there was very little, if any. There were 6 of them; 5 occurred in patients in whom the operation was in the upper abdomen, and the other (No. 5) was an infant who had pneumonia at the time (Table V, No. 1).

Circulatory depression is noted at four places in Table IX, and means in each instance that there was a fall in blood pressure concurrent with a rise in pulse rate, premonitory of shock. In each, ephedrine was given, and in each the circulation was evidently improved during the operation and for some time after. Eichholtz<sup>1</sup> found that the heart and blood pressure remained practically uninfluenced by a dose of avertin sufficient to produce ordinary anæsthesia, and Raginsky and one of us<sup>8</sup> have demonstrated the restorative action of ephedrine in avertin anaesthesia. From the point of view of the lethal effects of avertin, the cases of haemorrhage give us little concern, for the reason that they bled and avertin has nothing to do with this occurrence. Those who died from pancreatitis, intestinal obstruction or peritonitis were all very ill, and, we are convinced, would have died under any circumstances. The twenty-fifth case recovered completely from the effects of the anæsthetics, but death occurred six days later from uræmia brought on by obstruction in the urethra from carcinomatous growth. While it is true that the twenty-second case resulted in death three hours after operation, the patient nevertheless showed a tendency to recover from the effects of avertin, as evidenced by restlessness. At any rate, she was in a very cachectic condition on account of carcinoma of the breast, which was so advanced that it was fungating and

necrotic, the operation being performed for cosmetic and sanitary purposes.

It should be added that all of these 25 patients received oxygen and carbon dioxide post-operatively, as did the majority of the others of the entire series.

A careful and we think impartial analysis of these 25 cases convinced us, at any rate, that avertin could be exonerated from being more than a coincidence in these quite unavoidable mortalities.

We are pleased to note that others<sup>11, 12, 13</sup> who have used avertin extensively give equally eulogistic reports. We ourselves confess to quite definite enthusiasm.

#### SUMMARY

1. Avertin is a relatively safe anaesthetic and should be used more extensively.
2. Local anaesthetics should be used with avertin more frequently.
3. When nitrous oxide is being given together with avertin, oxygen may be administered

more freely than when nitrous oxide is being given alone.

4. Avertin does not cause nausea.
5. Doses of avertin should be greater than is customary.
6. Avertin should be administered slowly.

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### CORRECTIVE MEASURES FOR PROGRESSIVE DEAFNESS\*

By G. BERRY, M.D.,

Worcester, Mass.

**D**EAFNESS is a fairly universal ill. Perhaps 3 to 5 per cent of our children are hard of hearing: surely one out of ten of all adults suffers from this affliction. There are all grades, from a slight impairment to total deafness, from a handicap that spares until old age dims the lights, to the fettering oblivion which smothers the deaf child before speech can be acquired or education begun. In order to understand the better, at least, part of this broad and serious problem we can with advantage focus our attention. I am therefore inviting your scrutiny of the so-prevalent phase called progressive deafness.

#### PROGRESSIVE DEAFNESS

Progressive deafness in its typical form begins in adolescence. There is some dispute as to whether the incipient stage is not really in childhood. Many of us are contending that here is the onset and here the most hopeful point of

attack. The encroachment is gradual and therefore not realized until fairly well advanced. A 15 or even a 25 per cent loss may be reached before parents or friends are aware of the malady. As for the patient I may perhaps picture his own conception as that of remaining stationary while gradually the world of sound seems to be receding. Some of my hearers may have shared in this phenomenon. For such, the ear remains where it was, but certain sounds move farther away, the birds sing less enthusiastically, thunder does not intrude as often, people mumble their words more. Suppurative processes may superimpose and toxic complications intervene, but, excepting the accelerations they occasion, there continues the slowly marching insidious advance of the obstructive or catarrhal condition we are considering. With medical skill to help we may be able to hold things in check, and even make some gain, between the ages of twenty-five and fifty. Then senile changes begin and another steady decline may commence. In the earlier years, it is the

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low tones that are more affected. With toxic or senile changes the high tones slide off more. Not a cheering picture!

#### CORRECTIVE MEASURES

With this initial consideration of progressive deafness we turn to the corrective measures invited by our title. If any of you were seeking such corrective measures you would naturally and properly turn to an otologist. He is a trained expert, devoting his life seriously and continuously to understanding pathological processes involving the ear.—There is the surgical approach. The tonsils and adenoids may be causing recurring colds or Eustachian tube congestions; bad teeth may furnish their toxic handicap; a suppurative process in a sinus or in the middle ear may be adding its quota; a badly deviated septum may occasion faulty breathing. All these are amenable to skilled effort.—There is the medical approach. An allergic nasal mucous membrane may be contributing trouble; erroneous ingestion and faulty elimination may add to the burden; hygienic habits, supposed to be normal, may be quite at fault. He who would conscientiously serve such a patient must leave no stone unturned which will look toward finding and correcting any contributing factor.—But the average otologist is highly skilled. To the above suggestion that he look with more care and exert greater acumen, he may reply as the nobleman did to the Master: "All this have I done". If a temporary attack supervenes—an acute rhinitis, a congested tube, a retracted drum—our otologist will institute a series of treatments looking toward rectifying these errors. Success is attained and the temporary loss is restored. But further treatments may make the nose too roomy, or the tube too patent, or the drum membrane stretched and over-inflated. Before these can happen the usual conscientious doctor has said he has done his best and bids the patient goodbye.

It is just at this point in the wanderings of our discouraged patient and in the strivings of our conscientious otologist that the second phase of this discussion enters. What shall we do now? Is there no hope? These patients are scarcely ready to chant *morituri salutamus*. They are not yet prepared for their Nirvana. Their otologist has striven valiantly. Also, he has possibly received a considerable fee. He has tried every trick in the bag, employed every skill

at his command. But has he given of his wisdom and imparted from his store of experience that help which the patient so needs? There is further help available, not ideal, not what the patient expects or desires, but reasonably adequate, and a great boon to him who seeks and accepts it. These helps are in the nature of adjustments, not cures, but they are therapeutic in nature, just as much as is a druggist's prescription; and the otologist is the best initial agency for their application. I refer to the three important corrective helps of lip-reading, mechanical hearing aids, and psychological rehabilitation. Permit me to dwell for a moment on each of these important crutches for our limping patient.

#### LIP-READING

First there is lip-reading. Here the sense of sight tries to do double duty, and through an entirely different nerve approach, and by way of other brain paths, the speaker's idea is grasped. This means laboured and patient training. Brain centres do not accept and react unconsciously and automatically to new stimuli overnight. Long and tedious is the road our lip-reader must travel, but success awaits the winner and he who at last overcomes deserves and receives the crown. I wish you could attend with me the lip-reading tournament that will take place next month in Washington. The best will have come from the United States and Canada. You would marvel, and wonder how they can interpret sentence after sentence without error. But incredible as can be their accomplishment it is but a crutch, very worth while having, but not ideal. For instance, the lip-reader needs a good light on the speaker's face, lips that are not covered by a mustache, that move distinctly, and are neither over- nor under-active.

The fastest progress in lip-reading I ever saw demonstrated was in our Army School at Cape May, New Jersey. This responsibility gave me my first contact with this absorbing work; 108 war-deafened boys passed through our hands. They were sent to us for almost this sole purpose. Each had the undivided help of a skilled teacher for two and even three periods a day. They were saturated with lip-reading, and six to eight weeks of this intensive training saw many develop into expert lip-readers. It was interesting to note that a high mental development did not

necessarily help. Rather did the writer find an analytical habit of approach a distinct handicap when he took a few lessons. One ignorant Southern negro developed into a fine lip-reader, outstripping an officer and university graduate. The child usually learns more easily than the adult.—I wish there were time to dwell on this hard-of-hearing child problem, and to speak of the rapid growth of testing the hearing in the public schools; of the establishment of diagnostic clinics where the children can be examined, medical procedures advised, and corrective measures outlined; of the formation of lip-reading classes where the children attend two or three times a week and with this help can keep right on in their regular classes and in their normal environment, with a tremendous saving to the city treasury, and with renewed hope and comfort to the handicapped and discouraged youngsters.

#### THE EAR-PHONE

The second medium for help is the mechanical hearing aid. These are of varying types. Most are modifications of two forms — the trumpet, and the telephone, which we may call the ear-phone. The trumpet type may be used as a speaking-tube, taking the volume of sound direct to the ear, or it may be used as the reverse-end of a megaphone which carries the sound waves down the funnel to concentrate them at the ear piece. The major advantages of this type are that they are relatively cheap, they do not get out of order, and they do not distort the sound reaching the ear; the major disadvantages are the limitations and awkwardness inherent in their use, the extreme size needed to get any considerable magnification.

The ear-phone is more flexible. A very good rough test as to its adaptability to a given case is through the patient's own use of the telephone. A catarrhal patient may be quite deaf but be able to hear pretty well over the telephone. An ear-phone should help him. A patient with nerve deafness is likely to find adventitious sounds confusing. To him a conversation over the telephone seems jumbled. An ear-phone will be of questionable use to him.

Those who can use an ear-phone expect much of it. They ask it to pick up a clear voice from say fifty feet away, and to magnify it at the ear-piece so that it is loud and distinct enough to be understood by an ear that has lost perhaps

40 per cent of its acuity. Or, expressed roughly, they expect to hear conversation four times as far away as they can without the help of the instrument. The modern ear-phone can do that, thanks to the American Federation of Organizations for the Hard of Hearing and its members who have stimulated, to the altruistic geniuses who have invented, and to the artist workmen who have manufactured. But it has not yet reached perfection. It is too expensive. The actual making probably costs one-third to one-quarter of the final price. Some one must pay for the research work, for the advertising, for the many free trials, for the widely distributed agencies. It is delicate and gets out of order; the batteries become exhausted; the wire connections break. As a result, many a user has found his artificial hearing suddenly gone, and how he then wishes he could have the God-made variety back again! The instrument seems crotchety and fickle at times. In the hushed quiet of a beautiful concert it may cross-circuit and sing its own song, in shameful rivalry to the music of a Rosa Ponselle or a Fritz Kreisler. It distorts the sound somewhat and magnifies adventitious sounds as well, even to drowning out the sound we are listening to. The rattle of a program at a concert, or hand-clapping by one's neighbour, or the clatter of a dinner partner's fork on her plate, are deafening noises, for they are so near.—A word of explanation may help here. All of us have a threshold of audibility. This is at the silent end of our hearing capacity. At the loud end is the so-called "sensation point". At this latter point sound becomes so intense as to be felt; yes, it hurts. Varying hearing capacities have varying thresholds; but for all of us, whether hard of hearing or normal, our sensation points are about the same. When we realize this, we can understand that for the very hard of hearing the two extremes, the threshold of audibility on one end and the sensation point, on the other, are very near together. The margin is small. The ear-phone must keep within range. With magnification below that narrow range, I do not hear; with magnification above that range, the noise is unbearable. The manufacturer's task is not easy.

We have expected the same type of instrument to serve every need. A few firms are now realizing that the ear-phone should be adjusted to the individual, not the individual to the ear

phone. One effort was when the Sonotone Company developed its bone conduction ear-piece. They claim for it a clearer and less intense tone. This gave them two types of receivers; by air, and by bone. Now the Bell Telephone Laboratories have produced two distinct transmitters, one designed to help catarrhal or conduction deafness where the low notes are weakest, and the second to help the nerve or perception type where the upper tones are deficient. These are long steps in the right direction. As the manufacturer progresses we can conceive of three or even five different grades. Then, all the hypacusic patient will need will be a careful audiogram curve of his impairment, and the manufacturer will be able to send him the proper instrument. This happy day may be still distant, but those of us who have watched the evolution of the ear-phone find it rapidly drawing nearer. Now, with instruments so much better than ten or even five years ago, the inhibitions against wearing them are breaking down. Those who can manage without will find that they can do so much better with. Most of us could manage without eyeglasses, but how many do? General use and quantity production will bring the price within the reach of nearly all.

It has been suggested that the use of an ear-phone will rob the individual of the need of trying to hear and atrophy will result. This idea has been quite general, but has been proved untenable. Quite the contrary is the case. The hard-of-hearing person cannot hear as easily with an ear-phone as the normal can without one, but he does hear something. He strives yet harder to hear. If he takes off the ear-phone, he may hear nothing, and there is no longer the incentive for trying. Atrophy of disuse comes faster without than with this help.

Possibly a few concrete words of advice may help the potential purchaser of an ear-phone. Until standardization has advanced further the trial method must be followed. Try different makes. Some will best suit one, others another. Always take the instrument home and try it under normal life surroundings before buying it. Good companies understand this need. A nominal rental is properly charged which can be credited against the purchase price. The more expensive instruments are the more satisfactory in the long run. Try to secure one that

can use a standard dry-cell battery. It is cheaper, and can be secured readily wherever one travels. Good servicing is important. An ear-phone becomes as essential to one's happiness as does an automobile. It can ill be spared for shipping to a distant repair centre.

The above weak points have been explained because not to be forewarned of them finds the patient discouraged at the start. An ear-phone must be used like a garment before the strangeness can wear off. With this familiarity conversation that has been difficult becomes relatively easy. If the hearing is not too impaired, one can now resume many of the activities which were being curtailed. Not only is it easier for our friends to talk with us, but the world of sound returns again to a degree. The exquisite harmonies of a symphony orchestra, the laughter of children at play, the treasured voice of a loved one, are sorely missed if once taken away.

#### REHABILITATION

Our third corrective measure is the psychological. This was my chief theme before the Otological Section of the American Medical meeting last summer in Chicago. I can refer to it but briefly. As human beings we crave perfection. We are ashamed of an infirmity; this is axiomatic. The short woman wears high heels, the cripple tries to run. The hard of hearing deceive themselves and their friends as long as they can. This is natural. If it comes early in life the tragedy is there, but youth is resilient, especially if an understanding friend or a sympathetic parent takes his hand and leads the way. If the onset is in middle life, the man has his business contacts that make allowance for this disadvantage. He knows he is needed in the life around him; he finds daily opportunities for self-expression; he would like it to be different, but he carries on and is content. It is the woman who has the harder time. Her contacts are more superficial and more easily severed. She cannot be the jolly conversationalist that she used to be; it is harder to hold up her end in bridge, in club activities, or at the church; she finds it more difficult to entertain at her home; her husband seems to find it ever easier of an evening to enjoy his pipe and his book by himself. Slowly and cruelly her world contracts about her till, shut out of one thing and then another, she shrinks from every contact. First worry, then fear, finally despair, exact their toll.

Supersensitive, irritable, emotionally unbalanced, one trouble after another develops and there seems no relief.

One other type comes all too frequently. This is the deafness of advanced years. Here we have more impairment in the upper tones; here the ear-phone has not answered the need. The younger patient has a way out if he or she will take it, but the man of 65 travels untried trails with difficulty. Perhaps he is a man of affairs, his counsel has been sought in groups where weighty matters are discussed. He expected to serve as long as strength within him lay, is still rugged and strong, conscious of experiences and capacities for great and useful service; and yet, the world no longer has need of him. He is put away on the shelf long ere his time to stop has come. What then can he do? He suffers the "labour and sorrow" of the psalmist's four score years, and he is not "soon gone" and there is no "flying away". Fortunate is he if his rich life has built within him resources and springs which will continue to flow. Hobbies can delight; his pen can be just as vivid and entrancing; his family can the better know his profound philosophies; and, above all, she who has stood by him in sunshine can now illumine his shadow, and, each serving as a complement of the other, they can live gaily and serenely together through the ebbing years.

But it is the rehabilitation of those who lose their hearing while in their prime that I would emphasize. They are still young enough to be adaptable, to find their way out. For them especially are designed these corrective measures. The patient is beyond the help of tonics; surgical skill may offer no relief; but curative measures are available and the wise and broad-visioned doctor will seek them as eagerly and employ them as deftly as he will a drug or a scalpel. The art of lip-reading can be tackled and mastered by such as these. For them, an honest review of the situation, a frank confession of the infirmity, and a sensible conclusion to use the inventive genius of the ear-phone manufacturers, corrects in a large measure the handicap and rejoices the neighbour or partner or relative in being able to again have easy speech with his friend. Re-adjustments are hard, but they can be made. It is within one's own power, and happiness here, as elsewhere, is determined by one's own view-point.

One of the most effective agencies for the re-

habilitation I describe has been the American Federation of Organizations for the Hard of Hearing. I believe there are eight leagues in Canada, one here in Toronto, and other groups are forming, to join later the central Federation. There are over 130 of these leagues for the hard of hearing in America now, with memberships ranging from 25, to as high as 800. Here are gathered those who are determined to surmount their handicap. Here, both example and precept stimulate the newcomer out of his discouragement and into a determination to make the most of the many talents a bountiful Providence has blessed him with.

#### COMPENSATIONS

May I turn the page and dwell for a moment on the brighter side of the problem we are considering? Nature seems to delight in compensation. The wind-blown tree grows tougher bark and digs in more firmly with its roots. The northern animal grows a thicker fur. The bear's sight is poor but his very keen sense of smell early warns him of lurking danger. A Helen Keller's sense of touch is past our comprehension. The expert lip-reader can see and interpret facial movements that come and go ere we are aware of them. The pages of history teem with glorious accomplishments by the handicapped. Lord Byron, the cripple, swam the Hellespont; the divine Pavlowa had back trouble; the orator Demosthenes controlled a speech defect by placing a pebble under his tongue; the blind Milton saw visions, and the deaf Beethoven heard symphonies that will continue to satisfy a hungry world down through the ages. Most of us have a burden to carry, as had Christian in Pilgrim's Progress. Do not then be sorry for him who is hard of hearing. Rather, extend to him a helping hand. Bid him be of good cheer. Give him his "message to Garcia" and expect him to carry it through.

#### CONCLUSION

Permit me to close on this optimistic note. We have been discussing a different form of therapy than appears in our pharmacopœia. May I offer in compressed, shall we say, tabloid, form the following corrective measures? Perhaps one might be taken each night on retiring. They are not easy to digest and assimilate. It requires deliberate and earnest effort on the part of the patient. But given the will to do and the

courage to carry-on, I think you can promise him that sleep will be less troubled and the morrow's serener waking may find "the hill-side's dew-peared; the lark's on the wing;—all's right with the world". I have called them the Nine Commandments for the Hard of Hearing.

#### THE NINE COMMANDMENTS FOR THE HARD OF HEARING

I. Thou shalt frankly confess thy deafness to thyself and before thy fellow men. Let there be no deceit nor false pride.

II. Thou shalt not covet thy neighbour's hearing, but shalt rejoice that thou livest in an age when thy handicap can be made so small.

III. Early and again shalt thou consult thy otologist and accept every scientific aid he can render.

IV. Eschew the quack and his devices. Easy and broad is the way to his door and many there be that find it.

V. Thou shalt join and work for a League for the Hard of Hearing where thou wilt receive encouragement and stimulation for thyself and wilt find happiness in serving thy brother. Thus wilt thou march forward with the Federation army that is alleviating deafness throughout the world.

VI. So love thy neighbour that thou do everything in thy power to help him when he would have speech with thee. To this end:

VII. Thou shalt study lip-reading in season and out of season.

VIII. Thou shalt secure and use the best ear-phone thou canst discover.

IX. Triumphanty shalt thou rise above thine infirmity, and so conduct thy life that the world hath need of thee.

#### FUNDAMENTALS IN RECTAL DIAGNOSIS

By E. A. DANIELS, M.Sc., M.D.,

*Clinical Assistant, St. Mark's Hospital for Cancer, Fistula and Other Diseases of the Rectum,\*  
London, Eng.*

MEDICINE has been slow in accepting the investigation and treatment of rectal affections as its own responsibility, and thus rescuing from the hands of unqualified persons and the charlatan this important branch of the healing art.

#### RECTAL DIAGNOSIS

Rectal diagnosis, properly carried out, necessitates not only a knowledge of the normal rectum and the various abnormalities to which it is subject but also a comprehensive knowledge of general medicine.<sup>3</sup>

A short history should be taken, and this is often a useful preliminary. Since the examination is one of direct observation, the history is not of such great importance as in other branches of medicine. It is quite trying to obtain an adequate history from patients suffering from rectal disturbances. The duration of the symptoms is of importance. The majority of patients will come complaining of an external lump, pain

or bleeding. Bleeding is an important symptom, and its character and relation to stool should be determined. The habits and past medical history of the patient are of importance. This applies particularly to the use of alcohol and the presence of a tuberculous lesion in some part of the body. However it is usually quite impossible to obtain a satisfactory history in a rectal case, either because of modesty or lack of proper observation by the patient. The examiner will usually find that the most fruitful source of information will be a careful and painstaking examination.

Next to the index finger in importance, there are a few instruments the employment of which is essential to the performance of a complete rectal examination. Proper illumination is essential, either by a light with a focusing lens, a head light, or a terminal light attached to the proctoscope. Several proctoscopes of different sizes are needed, preferably one each of the following: a Gabriel, a Milligan and a Bensaude. These are all of the Kelly, short rectoscope

\* Prepared during tenure of assistantship—1933.

pattern. The Milligan and Bensaude are more tapering and of somewhat smaller bore. Since the proctoscope is only a few inches in length, as compared with the sigmoidoscope, one can gently pass it full length before withdrawing the plunger. Examination is performed during the withdrawal of the instrument. The patient should breathe through the mouth and not strain, until one is prepared to demonstrate the degree of haemorrhoidal dilatation (if any be present) and whether there is redundant mucosa.

Next in importance is a sigmoidoscope of either the Strauss (as used at St. Mark's Hospital) or the Yeomans' type. The latter has the advantage of having a concealed light at the proximal end of the instrument in a separate arm, which is a great convenience if the bowel is not thoroughly cleaned out. The Strauss sigmoidoscope is simple in operation, has a length of 30 cm., and is quite satisfactory. It may be observed that there are sigmoidoscopes for infants on the market. There is no reason why, with gentleness, the ordinary adult form cannot be employed in children over two years old. Infants may pass stools as bulky and consistent as that of an adult, and in examining children one can gently pass the standard Strauss pattern. Of course in children, because of the comparative straightness of the terminal bowel, one can reach into the sigmoid at a much shorter distance than in an adult. In children under two years of age, if sigmoidoscopy should be necessary, one of the instruments of smaller diameter will have to be employed. In performing sigmoidoscopy in children, because of the excitement induced, a general anaesthetic is always necessary. On the other hand a general anaesthetic is never necessary in doing an ordinary proctoscopic examination. It is advisable in proctoscoping children first to gently stretch the sphincter by passing the index finger, well lubricated, and to complete the examination by using a small Bensaude proctoscope, or an infant proctoscope of the Kelly pattern. The diameters of the Kelly, Gabriel or Milligan proctoscopes are larger than that of the Strauss sigmoidoscope, and these large instruments are therefore not suited for children.

A patient presenting himself or herself with rectal symptoms must receive a painstaking examination. This examination must commence with a careful inspection of the anal region and the surrounding ischio-rectal regions. The con-

dition of the peri-anal skin is important, and excoriations, undue redness or pallor, will immediately lead one to suspect that irritation has been present, either as a primary pruritus ani or secondary to some anal or rectal lesion. One should observe the patient's underclothing for soiling which will lead one to suspect inadequate control of the anal outlet. (One would rather refer to continence as being more dependent upon the anal outlet than upon the external sphincter alone, because the ano-rectal ring is now regarded as of almost equal importance). One should carefully look for any loss of symmetry, as slight bulging on one side of the anus or fullness of one ischio-rectal region will lead one to suspect suppuration which is presenting at the skin surface. It must be remembered that the focus may be *supra levatorem* or even in the pelvic bones. External palpation is an important aid to diagnosis and will reveal the induration of fistulous tracts, fluctuation, or induration in the later rectal zones, and the degree of sphincter tone. The finger should systematically palpate all around the sphincter and ischio-rectal regions. Moreover, such a preliminary palpation gains the patient's confidence, and after a few moments general relaxation and ease will replace an attitude of strain.

The finger is now gently passed into the rectum and this examination must be thorough. It should be done deliberately, keeping in mind the various anatomical structures which surround and lie in proximity to the rectum. In men, it is important to decide about the condition of the prostate and the seminal vesicles. In the female, it is nearly always possible to get a good deal of valuable information concerning the pelvic organs through digital examination of the rectum. Rectal symptoms may be due to one of many extra-rectal lesions. Proper invagination of the palpating finger at its metacarpo-phalangeal joint into the region between the tuberosities of the ischia is of far more importance than the actual length of one's finger. By gently and firmly invaginating one's index finger one can reach well into the ampulla of the rectum. Digital exploration of the anus, rectum and surrounding structures is a source of very valuable information if the procedure be carried out slowly and deliberately. During such an examination one should have a reasonable knowledge of what constitutes the normal. Haste in completing the examination is a great

source of error, and one should proceed slowly and at the same time review in one's mind the anatomical structures encountered. In passing, it may be here mentioned that one can never feel internal haemorrhoids unless they are thrombosed or have become polypoid. In order to determine their presence it is necessary to pass a proctoscope.

In conducting a proctoscopic or sigmoidoscopic examination the position of the patient is of great importance, if the procedure is to be completed without a struggle and with profit to the examiner. Improper or awkward positions will immediately handicap the examiner and render the examination difficult or impossible. For proctoscopy (by which one understands the passing of a short rectoscope of the Kelly, Gabriel or Milligan types, in contrast to a sigmoidoscope) the two desirable positions are the right or left lateral, and the knee-elbow. The knee-chest or knee-face positions will usually empty the haemorrhoidal veins, and in withdrawing the instrument one will be lead to believe that internal haemorrhoids are not present, when they may be truly present as a troublesome lesion. They actually have been emptied by passing the solid barrel of the proctoscope over them, and kept emptied by the almost inverted position of the rectum secured by the knee-chest or knee-face positions. If such a patient be placed in the lateral or knee-elbow positions, one may be surprised, on withdrawing the instrument and asking him to strain gently, at the presence of a large haemorrhoidal ring prolapsing into the lumen of the instrument.

Sigmoidoscopy can be converted into a simple office procedure. The art of performing a successful sigmoidoscopic examination depends upon a few simplicities. Firstly, the patient should not be prepared by purgation, or forewarned, so that he comes trembling to the physician, expecting the worst; secondly, he should never see the instrument; and, thirdly, and most important of all, the proper position of the patient during examination. One loses a great deal of valuable information if the patient comes prepared by preliminary purgation and wash-outs. The object of sigmoidoscopy is to examine the rectum and sigmoid in as undisturbed a state as possible. Preliminary purgations and wash-outs produce congestion of the mucosa, generally wash away secretions, and induce a condition of irritability and even spasm of the sigmoid and rectum—

conditions not conducive to an easy examination. How often has one observed sigmoidoscopic reports of a congested mucous membrane which is really the result of preliminary purgation and wash-outs. It is best, if possible, to see a case for sigmoidoscopy in the afternoon, because most persons have a bowel movement in the morning. At the very most one may order a mild aperient pill, to be taken at bedtime. If some faeces are present, this is no bar to examination, as the instrument can sweep around them in most cases. If the ampulla is hopelessly loaded, the patient should be asked to return in a few days, when one will usually have better fortune. It cannot be stressed too strongly that one must try to examine the rectum and sigmoid in their normal states, even if some faeces are present. Moreover the colour and consistency of the bowel contents are important in appraising the case.

In order to pass the sigmoidoscope smoothly and easily the true pelvis must be emptied of coils of small intestine, and the rectum and sigmoid inverted as much as possible. This is only possible by careful posturing of the patient into the knee-chest, or better the knee-chest-face, position with the small of the back well hollowed out. The knees are spread apart. A solid table lends assurance to the patient. It is well worth one's while to spend several moments posturing a patient before commencing the examination. In the knee-elbow or lateral positions the pelvis is usually filled with loops of small bowel and in passing the instrument the patient will suffer much. The instrument is passed under direct vision, the plunger being withdrawn as soon as the sphincter is passed. It is not necessary to distend the bowel by making too frequent use of the attached rubber bag inflater. A slight pump occasionally will suffice, thus displacing the bit of redundant bowel ahead a little at a time. One should ordinarily be able to pass the instrument to a distance of between 20 to 26 cm. without any difficulty. One thing must be pointed out concerning sigmoidoscopy. *Every patient cannot be sigmoidoscoped* (any more than one can cure every fistula without producing incontinence). About 5 per cent of people, because of anatomical reasons, whether this be a very marked promontory of the sacrum or a short mesosigmoid, cannot be sigmoidoscoped. This fact must be known if one is to avoid damaging the bowel. It is better to try again

than to make the patient suffer and traumatize the intestine.

Sigmoidoscopy, properly performed, whilst somewhat annoying and uncomfortable to the patient, should not produce suffering, and if this follows one should desist immediately. Anæsthesia is very seldom needed in any form, and making this method of examining the bowel a simple office procedure will mean that cancer will be more often detected in a portion of the intestinal tract which is frequently the site of malignant lesions.

In rectal diagnosis one cannot over-emphasize the importance of a complete examination in every case, which should include the bowel from anus to sigmoid. The reason for this is the occurrence of double lesions. A patient with an anal fissure may have an ampullary cancer as also may the one with haemorrhoids. A barium examination may also have to supplement the sigmoidoscopic examination. Moreover, a patient may have an ampullary growth with a second growth in the sigmoid. This is often the case where malignancy has been superimposed upon a benign adenoma. Since adenomata are usually multiple, the occurrence of multiple malignancies should be kept in mind.

One can now pass on to the consideration of the various symptoms in cases suffering from rectal disease.

**Pain.**—One can say at the outset that any patient presenting himself with rectal pain of a severe character will usually be the subject of a lesion below the pectinate line. When a lesion is present above the pectinate line pain is seldom present. Instead the patient presents other symptoms, such as a troublesome discharge, backache, a feeling of fullness in the bowel, some degree of tenesmus, straining after stool, or digestive upsets. This relative absence of pain in lesions above the pectinate line is unfortunate, because of the late diagnosis of cancer of the rectum in many cases; and again it calls for the most searching examination of the rectum and sigmoid in any obscure case. No patient with anaemia, dyspepsia, back-pain, or constipation should be discharged without a complete rectal examination. It is not sufficient merely to pass the finger, because only about 50 per cent of rectal carcinomata are within reach of the average index finger, and if proper invagination of the finger is not exercised this percentage will be considerably reduced.

The most painful of all ano-rectal conditions is dorsal fissure of the anus. In about 95 per cent of the cases this lesion is present in the posterior aspect of the anus, usually in the mid-line, but it may be slightly lateral. The pain is exquisite and is accompanied by spasm of the external sphincter. In chronic cases, after the formation of the sentinel pile there is actual fibrosis of the external sphincter and its surrounding connective tissue. Such a case will present an anus beyond which it is quite impossible to pass one's finger, no matter how gently one proceeds. It is now advisable to desist, and a complete examination deferred to a future date. Meantime the fissure is demonstrated by urging the patient to relax, and by gently retracting the anal margins. The patient is now asked to bear down. In nearly all cases, at the posterior aspect of the anus, very near the mucocutaneous border, a small acutely inflamed ulcer will be found. This may be undermined at its base and have a submucous abscess extending above it. The lesion bleeds easily. Except in chronic fissures there is very little induration.

A differential diagnosis of anal fissure is important, because this lesion may be confused, especially in its chronic states, with anal chancre, epithelioma, or anal tuberculosis. A tuberculous ulcer of the anus will fail to respond to local treatment, and the ulcer will gradually enlarge and present undermined margins. Primary chancre of the anus early shows marked induration of its periphery, which is never observed in a fresh fissure. The inguinal glands quickly enlarge, and the Wassermann reaction becomes positive very early in primary sore of the anus. A fissure of many weeks' standing has many of the appearances of primary chancre of the anus and the differential diagnosis is often a very subtle one. Primary syphilitic lesions of the anus are not uncommon, and one should never overlook their possibility. Dark field illumination of a scraping from the ulcer surface is valuable. Squamous carcinoma of the anus may resemble a chronic fissure (often also quite indurated). Microscopic examination of a snipping is the only certain method of completing the diagnosis in such doubtful cases.

Submucous abscess of the rectum produces a dull throbbing pain, felt low down in the rectum. This is the result of a fissure, cryptitis, and fistulae whose drainage may have become arrested. Fever may be present, and one can feel a cord-

like induration extending up from the anus, which is exquisitely tender.

Another frequent cause of rectal pain is an anal haemato-ma, better known as an "external thrombotic pile". This presents at the anal margin as one or more blue tense swellings containing blood clots. It comes on suddenly, and the pain and discomfort are distressing. Simple inspection of the anus provides one with the diagnosis.

Internal haemorrhoids which have become prolapsed and swollen will produce severe pain. The sphincter will, through its spasm, "choke off" the prolapsed haemorrhoids, and necrosis, sloughing and infection will ensue. It is extremely rare and almost unknown (Gabriel), for sloughing thrombosed infected piles to lead to portal pyæmia. The writer recently observed a patient, admitted to hospital, with a large mass of sloughing necrotic prolapsed piles. The patient was toxic and there was great abdominal distension, with icterus of the conjunctivæ. Fever was high and the respiratory rate increased. The liver was slightly enlarged and tender on palpation. A diagnosis of portal pyæmia and septicæmia was made. The patient died soon after admission, and at autopsy the liver showed no sepsis and the portal system was normal. There was consolidation of the right lower lobe of the lung, which dullness at examination, because of the absence of pneumonic symptoms, was taken to be upward enlargement of the liver compressing the lung. The early cough no doubt brought the haemorrhoids down and sloughing ensued. Cough in this case was no longer present on admission, no doubt because of great toxicity; and the downward enlargement and tenderness of the liver were no doubt cardiac in nature. Therefore in sloughing necrotic piles, with signs of sepsis, one should make a thorough search for a pneumonic lesion.

The continued ingestion of saline cathartics, with the long-continued passing of liquid stools, will produce a red congested anus and a spasmodic or even fibrous sphincter. Some pain and much irritation will ensue.

Another cause of rectal pain is the injudicious injection of haemorrhoids, either by incorrect technique or injecting cases not suitable for such treatment. Upon examination, one may observe an infected ulcer of the rectum with submucous or pararectal suppuration. One must never fail

to enquire about previous treatment in any case of rectal ulceration or infection.

Amongst other causes of rectal pain are the impaction of foreign bodies into the lower rectum, such as bits of fish, or chicken bone and peri-rectal or peri-anal suppuration. Injudicious prostatic massage, rectal ulceration from cervical radiation, and sodomy or impalement of the rectum are rarer causes of rectal pain. The taking of a careful history and the performing of a thorough examination will soon demonstrate the cause in such cases. Proctitis, whether gonorrhœal or non-specific seldom causes rectal pain.

Rectal cancer is seldom a painful lesion, and actual pain only occurs if the cancer extends down below the pectinate line and involves the anus. Lateral spread also causes late pain. Other troublesome symptoms, rather than pain, are characteristic of cancer of the rectum.

*Bleeding.*—Bleeding from the rectum is most commonly caused by internal haemorrhoids, and fissure *in ano*. In the former the stool may be spattered, only if there is sphincteric spasm. Where the sphincter is patulous, as the result of prolapse of the piles, a trickle of blood will occur with and also between stools. On passing a proctoscope in a case of piles of long standing, one is often impressed by the marked pallor of the rectal mucosa, evidence of a secondary anaemia. The methods already described will be employed to diagnose haemorrhoids and fissure *in ano*. Fissure *in ano*, even in its chronic variety, may cause free rectal bleeding. Rectal cancer does not as a rule cause bleeding until the lesion has become advanced enough to produce central sloughing and ulceration of the growth, and therefore one must not regard bleeding *per rectum* as an early symptom of rectal malignancy (Duke's classification of rectal cancer).<sup>4</sup>

The benign tumours of epithelial origin, adenomata and papillomata, may cause free rectal bleeding. Sigmoidoscopy will reveal these lesions. The former are seen as one or more sessile swellings in the sigmoid and upper rectum, of a deeper red colour than the ordinary mucous membrane. The papillomata are soft villous growths, which bleed freely. One must mention the unfortunate disease, "Familial polyposis intestini", which may run through several or many generations of the family, and which is characterized by bleeding and anaemia

coming on in the early 'teens or twenties. Malignancy invariably ensues, and the prognosis is a very sad one. The disease is hereditary, and the writer has seen the charts of a number of families, traced through several generations, in which many of its young members were decimated as the result of malignancy superimposed upon this condition. This disease must be differentiated from the non-hereditary type of multiple adenomatosis intestini which also has a great tendency to undergo malignant changes. These causes of rectal bleeding will always be diagnosed by a careful examination.

Acute proctitis may cause free bleeding *per rectum*. Amongst other causes one must bear in mind peptic ulceration, intussusception in children, and ulcerative lesions of the colon. Bleeding *per rectum* has been observed in cases of Meckel's diverticulum. Such bleeding has been demonstrated as coming from areas of ulcerated aberrant gastric mucosa in these cases. Diverticulosis of the sigmoid, even with superimposed infection, never or very rarely causes rectal bleeding.

*Rectal irritation.*—Rectal irritation may be the result of any of the lesions already enumerated. Except in the presence of pin-worms, where there are no demonstrable rectal or anal lesions pruritus ani must be regarded as a neurosis calling for symptomatic treatment. In

many cases some rectal lesion will be responsible for a tiresome itch. The commoner exciting causes of peri-anal irritation are external tags, and a relaxed sphincter due to prolapsing piles, resulting in constant moisture because of a mucoid leak, and the ingestion of liquid paraffin in large doses. Peri-anal skin changes always speak for a long-standing irritative condition.

#### SUMMARY

Rectal symptoms call for a complete painstaking examination by the physician or surgeon. A correct diagnosis will always reward the examiner who is prepared to carry out a deliberate and searching examination. Digital examination of the rectum, not supplemented by other methods of investigation, is quite inadequate in diagnosing rectal disease. The mortality from rectal cancer can be signally reduced and many more cases brought within the operable group if the physician and surgeon will conscientiously investigate every case presenting rectal signs and symptoms by the methods enumerated in this thesis.

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#### THE TREATMENT OF DIETARY ANÆMIA\*

BY CHARLES E. SNELLING, M.B.,

*Toronto*

IN a former communication<sup>1</sup> it was stated that dietary anæmia could be cured with iron in adequate amounts in an assimilable form. The present report shows the results that were obtained with a group of patients treated in the Out-Patient Clinic.

In spite of numerous investigations<sup>2 to 8</sup> showing the value and action of iron and, later, copper, as well as some of the other metals, in the treatment and cure of dietary anæmia, a large number of clinicians still remain who do not adopt this form of therapy. Lucas<sup>2</sup> advises the feeding of iron-containing foods in the mild

cases, but small repeated transfusions in the more severe. He states that iron in various forms should be tried, but that not so much benefit can be expected from this form of therapy as was formerly supposed. Until recently the practice in this clinic has been to give one or more transfusions until the haemoglobin approximates the normal level, having the patient under observation in the hospital. The results have been satisfactory, in that the anæmia is relieved, and from that time the infant usually eats a normal diet and has no recurrence of the anæmia. However, the admission of patients to the hospital and transfusion are an expense to the parents or the State.

\* From the Department of Paediatrics, University of Toronto, and the Hospital for Sick Children, under the direction of Alan Brown, M.D., F.R.C.P.(C.).

Parsons and his co-workers<sup>3</sup> showed that yeast may have some stimulating effect on the iron in the recovery from dietary anæmia. They show in their graphs some very rapid increases in the haemoglobin values. Josephs<sup>4</sup> found that iron ammonium citrate brought about a rapid rise in haemoglobin to 60 per cent, and from that point the rise was slow. If copper sulphate was also added the rise continued to 80 per cent before it became retarded. Blackfan, Baty and Diamond<sup>5</sup> advocate a well-balanced diet, with small repeated transfusions in the more severe cases. They also use iron and ammonium citrate in 3 to 4 gram doses daily with very beneficial results.

This paper reports the results from 10 consecutive patients with dietary anæmia treated

with iron in the Out-Patient Clinic. In the Table are found the essential details of the history, weight, progress and dosage of iron and ammonium citrate, which was dissolved in the milk feeding for the whole day. The haemoglobin was estimated by the Sahli method, and smears were taken. In the majority the haemoglobin was rechecked at a period of from one to two weeks after commencing treatment, and then at one to two months.

The diagnosis of dietary anæmia was made from the history, the haemoglobin value, and the appearance of the smear. Dietary anæmia is of a hypochromic type, with a low colour index. In the smear the cells are seen to be poorly filled with haemoglobin.

The birth weight was known in 9 of the 10

TABLE

Case	Birth-Weight	Date	Age	*Iron and Ammonium Citrate Amt. Daily	Remarks	Weight	Sahli Hgb.
1	6 lbs. 13 ozs.	Mar. 27/33 Apr. 3/33 May 1/33	12 mos.	2 drams 1 dram 1 dram	Pallor, anorexia; milk diet. Colour better, appetite excellent. Walking and eating well.	25 lbs. 28 lbs.	Per cent 32 65 75
2	6 lbs. ½ oz.	May 19/33 June 30/33	15 mos.	½ dram ½ dram	Not eating; pallor; hæmic murmur and enlarged heart. Eating well, colour good.	21 lbs. 22 lbs.	38 68
3	4 lbs.	July 27/33 Oct. 2/33	12 mos.	1 dram	Drinks milk; looks pale. Colour good; eating well.	17 lbs. 19 lbs.	47 80
4	3½ lbs.	Dec. 1/32 Dec. 19/32	9 mos.	1 dram ½ dram	Pallor; will not eat solid food. Cold, looks better; not eating too well.	15 lbs. 8 ozs. 15 lbs. 12 ozs.	50 70
5	4½ lbs. (twin)	Mar. 9/33 Mar. 16/33 Apr. 3/33	11 mos.	1 dram 1 dram ½ dram	No solid food; pallor. Much improved. Eating well; colour good.	18 lbs. 14 ozs. 19 lbs. 4 ozs. 23 lbs. 8 ozs.	40 80
6	?	Aug. 10/33 Sept. 14/33		1 dram 1 dram	Pallor; 4 months ago had been put on spinach, apricots, eggs. Colour good; eating well.	23 lbs. 26 lbs.	50 80
7	6 lbs.	May 1/33 May 8/33 June 15/33	17 mos.	2 drams 1 dram 1 dram	Refuses solid food; pallor. Eating everything; colour better. Eating everything; normal child.	20½ lbs. 21 lbs. 22½ lbs.	33 65 85
8	2½ lbs.	June 26/33 July 24/33 Aug. 8/33 Aug. 28/33	10 mos.	2 drams 1 dram irregularly 1 dram irregularly 1 dram	Pallor; listless; anæmic.  Colour good.		38 52 60 80
9	5 lbs. (twin)	Feb. 16/33 Feb. 23/33 Mar. 2/33	9 mos.	1 dram 1 dram 1 dram	Pallor. Looked better. Looked well; eating.	14 lbs. 14 lbs. 10 ozs. 15½ lbs.	50 70
10	4 lbs.	Apr. 7/33 Apr. 21/33	2 yrs.	1 dram 1 dram	Pallor; hæmic murmur. Eating better.	26¾ lbs. 27½ lbs.	37 52

\*The iron and ammonium citrate in this series was obtained from Merck & Co., and British Drug Houses, Ltd. Repeated analyses in our Laboratories have shown no traces of copper.

Merck & Co.'s analysis shows 16 to 18 per cent iron and not more than 0.004 per cent copper.

cases. In 6 of these it was 5 pounds or below, which indicates that 66 per cent were premature infants. The age at which treatment was sought for the condition in the full-term infants was from 12 to 17 months. In the prematurely-born infants it was, with one exception, under one year. It has been found that any infant, regardless of the period of gestation, contains 3 times as much iron in proportion to its weight as a child over 1 year of age.<sup>6</sup> In other words, the new-born child can triple its birth weight without developing anaemia, on a milk diet, which of necessity is low in iron. The prematurely-born infant triples the birth weight at less than 1 year of age, and the full-term at one year, on an average. Anaemia should not develop until after that point in development is reached. This small series of cases supports this view.

The history and findings on the first visit were the same in practically every instance. The children had anorexia; milk was the sole food, and solids were refused. They showed pallor and listlessness, and a haem murmur was found in many. The haemoglobin values ranged from 32 to 50 per cent. After the feeding of iron ammonium citrate in the formula marked improvement was invariably noticed. The mothers reported that the infants began to eat solid food with enthusiasm, without coaxing or forcing, and became active and energetic. The colour improved and there was a noticeably rapid gain in weight. The haemoglobin values are recorded. In the two with the lowest initial percentage there was 100 per cent increase in the haemoglobin in 1 week, after which the rise was slow. In most instances where the observation was made early, it was found that the initial rise was very rapid to approximately 65 per cent, and the subsequent rise took a period of one to two months.

Iron<sup>7</sup> is absorbed from the gastrointestinal tract in the ferrous form. Iron and ammonium citrate in the stomach is changed to ferrous and ferric chloride. The proportions of these two depend on the amount of reducing substances in the food. If the reducing substances in the food are increased the proportion of ferrous salt is raised. A mixed diet containing meat and vegetables has a large quantity of reducing substances, and so with this diet the proportion of ferrous chloride is high when iron is administered. Likewise, the amount of

ferrous chloride formed in the stomach varies directly as the amount of iron present. In other words, small amounts of iron and ammonium citrate will gradually all be changed to ferric chloride or the unavailable form. If, however, a larger quantity of iron and ammonium citrate is given, the proportion of the ferrous salt is raised. This explains the necessity of such large doses as advocated in this report.

In animal experimentation large doses of ferrous chloride cause vomiting, diarrhoea, diuresis, and anorexia. If the total quantity of iron and ammonium citrate administered here were changed to ferrous chloride undoubtedly there would be toxic symptoms. However, a milk or milk and cereal diet contains only small quantities of reducing substances, so that the quantity of iron must be high to have the ferrous salt formed. No toxic symptoms were observed in any of the patients treated in this series, although diarrhoea has been observed in some older children where the diet was more varied.

When such rapid and striking results as these can be obtained with the quantities of iron used here, it would seem that unless there is some other reason for transfusion, this is not necessary in the treatment of dietary anaemia. Treatment by iron is much less expensive, more easily administered, allows the child to produce a natural cure, and obviates the danger of cross-infection. If, however, infection is present, immediate transfusion is indicated to raise the resistance, and this should be followed by iron therapy.

In the pharmacopoeia the adult dose for iron ammonium citrate is given as 5 to 10 grains. If proportional doses are used in infants the results are bound to be poor and there will be a slow response. In these patients 60 to 120 grains daily have been used at the commencement of treatment. Due to its extreme solubility this is an excellent form of iron to use, as it may be administered to infants in the formula or in any other fluid vehicle that is taken readily, such as orange juice.

#### SUMMARY

Ten cases of dietary anaemia were treated with iron and ammonium citrate in doses of 60 to 120 grains daily, which was dissolved in the milk feeding for the day. This was found to be

a convenient form in which to give iron. No untoward effects were observed from the use of the large doses prescribed.

There was a rapid improvement in the appetite, activity, colour, weight, and general physical state of each infant. The haemoglobin rose very rapidly for the initial period, and subsequently slowly approached the normal level.

When such rapid and striking improvement can be obtained with iron alone the necessity for the use of transfusions in the treatment of dietary anaemia is greatly diminished, unless indicated by some complication.

Sixty-six per cent of these infants had a birth weight of 5 lbs. or less. In this group the anaemia developed in the last quarter of the first year. The full term infants did not ap-

pear for treatment of the anaemia till after 1 year of age.

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## SPINELLI OPERATION FOLLOWED BY PREGNANCY AND LABOUR

By W. PELTON TEW, M.B., F.R.C.S.(Ed.), F.R.C.S.(C.), M.C.O.G.,

*London, Ont.*

NORMAN F. MILLER<sup>1</sup> in 1927 collected 55 cases from the literature and reported one of his own of inversion of the uterus followed by pregnancy. In this group of cases the youngest patient recorded was 18 years of age. The original inversion existed six weeks before it was repaired by Piccoli's incision. Two subsequent pregnancies occurred, both terminating normally. The oldest patient in Miller's group was 37. There were 16 primiparæ and 21 multiparæ; the parity of the rest of the group was not stated. Fifteen of the group were corrected immediately. The average duration for the whole group was 33 days. The longest interval was 12 months. Four of the group underwent spontaneous replacement after several attempts at manual replacement. The average duration of the inversion for these cases was nine months; the longest duration in any one case was five years.

The 55 cases reported by Miller were corrected as follows. Twenty-five were replaced manually; 8 underwent spontaneous replacement; 22 were corrected by operation. Eight of the operative corrections were made by Piccoli's method; two by the combined Piccoli-Borelius-Westermann method; three by the Kustner operation; five

by the Spinelli operation; one by the Kustner-Borelius-Westermann operation; one by Kehrer's method, and one by Duret's method.

Inversion did not recur in subsequent pregnancies among the 22 cases corrected by operation; it occurred 11 times in the 25 cases corrected manually. There were only three cases of subsequent abortions among the cases reported. Adherent placenta occurred in the subsequent pregnancies in 40 per cent of the cases corrected manually, and in 18 per cent of the cases corrected by operation. Twenty-nine confinements were reported afterwards in the 22 cases corrected by operation. Uterine rupture did not occur in any case.

From this report it would appear that conservative management of pregnancy and labour is the method of choice for cases of pregnancy following corrected uterine inversions. This holds true for cases manually corrected and for cases corrected by operation, providing the post-operative convalescence is afebrile. The possibility of rupture of the uterus should be kept in mind, but seemingly the chances of it occurring are not very great.

Miller reported 22 cases of pregnancy and labour following operative correction of uterine

inversion. Of this group 5 cases were corrected by the Spinelli operation. The following case was corrected by the Spinelli operation.

Mrs. C.B., aged twenty-nine, presented herself at the out-patient Gynaecological Clinic, Victoria Hospital, London, Ont., on February 25, 1931. Her past history was as follows. She was confined with her first baby in Ottawa. The record of this confinement was not looked up. Her second confinement was on October 15, 1927, in Victoria Hospital, London, Ont. This labour lasted five and a half hours. The delivery was spontaneous and the baby weighed seven pounds ten ounces. The mother and baby both left the hospital under normal circumstances on the tenth day following labour. She was then a semi-private patient. Her third confinement was on March 3, 1929. This labour lasted four hours and the delivery was spontaneous. The following is a quotation of the house-surgeon's notes concerning the delivery of the placenta. "On expression of the placenta by Crédé's method it was found very adherent. On traction a mass was brought forward the size of an adult fist. The membranes were separated and the placenta delivered. A hand was inserted into the uterus and a submucous pedunculated fibroid (?) growing from the posterior wall of the fundus was found."

Some of the nurse's notes on the history were as follows. "Placenta expelled with difficulty. Ergot, one ampoule, and pituitrin, one ampoule, given. Considerable haemorrhage; pulse weak at times. Condition fair as patient was moved from the labour room to her own. Two hours after delivery the perineal pads were quite saturated. No complaints of pain. Five hours after delivery pulse rather weak; condition fair. The following morning there was no severe flowing." From then on the flowing gradually decreased. The mother nursed her baby. The patient was discharged from the hospital on the twelfth day with a normal temperature and a pulse rate of ninety. Her average temperature was about 100° and her average pulse rate about 100 during the eleven days following confinement.

The patient stated that after leaving the hospital a mass protruded from the vagina when she was on her feet. This mass gradually decreased in size and

receded. It finally would appear only during her menstrual periods. A diagnosis of a completely inverted uterus was made and the patient was admitted to the Indoor Service. She was menstruating on the day of admittance to the hospital. The inverted uterus was protruding through the vulvar orifice, and we had the opportunity of observing the interior of the uterus weeping droplets of blood during a menstrual period. There was a moderate amount of flowing on February 26th, 27th, and 28th. On March 1st there was very little flow; on March 3rd the period was over. There was a pinkish discharge for the next two or three days. The uterus gradually receded into the vagina. The patient stated that the uterus (or mass) had been protruding in this manner with each of her menstrual periods during the past two years. On March 12th I performed the Spinelli operation. On March 30th she was up for the first time and was discharged from the hospital on April 3rd with the pelvis very satisfactory.

On leaving the hospital the patient was requested to return to the Out-door Gynaecological Clinic periodically for examination. She was also advised to avoid pregnancy for about one year. The subsequent examinations of the pelvis proved it to be comparatively normal; her menstrual periods were perfectly normal.

On November 30, 1933, the patient presented herself at my office stating that her last normal period was April 28, 1933. On examination I found her to be about seven months pregnant, and I arranged for her to attend the pre-natal clinic. She was confined on December 30, 1933. The duration of the labour was four hours and the delivery was spontaneous. The baby weighed five pounds, two and three-quarter ounces. This was no doubt due to the fact that labour began about three weeks prematurely. The baby was vigorous and did well from birth. The placenta came away rather reluctantly at the end of an hour, with the help of the Crédé method. The puerperal period was normal, and on discharge from the hospital on the fourteenth day after delivery the uterus was well involuted and the pelvis seemed normal.

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## THE ROLE OF THE PATHOLOGIST IN THE DIAGNOSIS OF CANCER\*

By W. L. ROBINSON, M.B.,

Toronto

"THE rôle of the pathologist in the diagnosis of cancer"; I am glad the subject is stated thus and not as "The rôle of the microscope", or "The rôle of the laboratory". The human element, the pathologist, is recognized. In these days of delicate instruments of superb scientific exactitude and serological reactions of almost unbelievable accuracy, we are prone,

I believe, to rely unduly upon things mechanical and chemical and to forget the humanism in things scientific and religious. The world has been dominated, says Whitehead, for three centuries by science. This is reflected in our materialistic concepts of everyday life and our faith in the reality and certainty of matter. The modern physicists and philosophers, however, are showing us the uncertainty of such concepts, and are emphasizing the importance of mind and the concrete reality of its existence. And so while we have today at our disposal beautifully equipped laboratories, with machines for cutting sections film-like in

\* A paper read before the combined meeting of the Section of Pathology with the Section of Surgery, Academy of Medicine, Toronto, on January 24, 1933.

Earlier articles in the series on the diagnosis of cancer can be found in the *Journal* as follows:—1933, 29: 465; 1934, 30: 46, 48, 50, 168, 171, 280, 283, 522, 639; 31: 9, 165.

thickness, an almost endless variety of dyes for staining them, and microscopes that would have delighted beyond measure the heart of Virchow, we are still dependent for the diagnosing of pathological material upon the human element. I do not wish, however, to belittle those physical accessories which combine to make our modern laboratories so efficient and delightful to work in. They are a very important part of the scheme, and in the stress of modern medical diagnosing are becoming more and more of a necessity.

The study of morbid histology was begun less than one hundred years ago. Much was expected of it, particularly in reference to the study of tumours, and, while it has failed to answer all of the questions, it has contributed more to our knowledge of tumours than any other method. But it has its limitations, and for this reason will not be likely to contribute anything further of a dramatic nature to the advancement of our knowledge. To those, however, who recognize its limitations it has a great deal more reliable information to impart than any of the more modern and much boasted biochemical and biophysical methods of present-day investigation. Its technique is sound, but not thrilling; exacting, but not infallible; scientific, but not materialistic.

The pathologist, like the radiologist and the surgeon, in approaching his problem must have a background of experience and of training in the appreciation of the normal, such as the embryological development of the body, the histological appearances of the various cells and tissues which go to make up that body, and the ability to evaluate the limits of physiological change which occur in those tissues. In other words, this means a good understanding of the normal. He must then have behind him reliable technicians and assistants and the best mechanical equipment that can be afforded. He must have a thorough understanding of the whole process of tissue-embedding, sectioning and staining. Technique is something that can very seldom be left to the technician. A constant check has to be kept on this work. Many a poor diagnosis can be traced back to faulty technique. Such being the case, no effort should be spared to keep it up to as near the perfect level as possible.

The gross features of the tumour are next to be considered, and here let me say that I think

it probably just as important for the surgeon to have an appreciation of these as it is for the pathologist. We are absolutely dependent upon him many times for the choice of representative pieces of tissue. To do this intelligently he must have an understanding of the gross appearances of tumours and the characteristics of their growth. For instance, a block taken from the centre of a growth is often valueless. A piece scraped off the top is not only very difficult to handle from a technical standpoint, but is usually very inconclusive and trying on the nerves of the pathologist who is called upon to assume responsibility for the diagnosis. When a goodly portion, or the whole of the tumour, has been submitted the choice of blocks then lies with the pathologist. Under such circumstances the difficulties of diagnosing become largely histological. The gross features, moreover, play their part in indicating leads along which the mind can travel in its search for the solution of the problem. The surgeon by sending to the pathologist good representative portions of the tumour relieves himself of considerable responsibility, and makes it much easier for the pathologist to proceed with his study. Just a word here about biopsies. A biopsy or the removal of a portion of tumour growth from the living body is generally considered now to be a fairly safe as well as sound procedure, providing that in cases where malignancy is diagnosed treatment is not too long delayed, say not more than a week or ten days.

While we are on the subject of sending things to the pathologist I should like to rectify a false impression which we sometimes believe exists in the minds of clinicians, *viz.*, that we are independent or above the need for clinical assistance in the way of historical facts of the case. I have known clinicians to express a desire to withhold all history of the case, fearing that it might bias us in the formation of our opinion. Of course this is true, but not in the sense in which it was meant. Sometimes it simplifies things tremendously to have some idea of what the problem is from a clinical standpoint. Such things as the age and sex of the patient, duration and location of the growth, whether or not there had been previous x-ray or radium treatment, and whether or not an operation had recently been performed. All these give us a setting in which to place our problem, and from it we can very much more intelligently approach

it and offer you in return dividends incomparably better than if otherwise conducted. After all, the diagnosing of tumours should not be allowed to degenerate into a game of mental gymnastics or a battle of wits between clinician and pathologist. We are all working for the one end—the ultimate good of the patient. Pride in our skill must take a subsidiary place.

We come now to the microscopic examination of the tumour. We are enabled here to learn something of the detailed structure of the growth in question. Inflammatory lesions, traumatic reactions, and physiological hyperplasia have to be eliminated. As a rule these are readily recognized. Sometimes, however, they present a very difficult problem which is confusing and hard to solve. Lymphosarcomata and some of the endotheliomata are examples of such conditions. At times it is with considerable difficulty that we are able to distinguish these from inflammatory reactions.

In the case of a true tumour we are able by the use of the microscope to identify cell structure, cell type, and cell differentiation. This however, is not always a simple procedure. While there are certain fundamental characteristics of malignancy, these are not all necessarily manifested in the one growth. The variability of cell types also increases the difficulty of our problem. There are some fifteen to twenty different types of cells in the body, any one of which may give rise to a tumour. There is also a variability in cell differentiation within each group of tumours.

The pathologist recognizes very early in his career that there is no standard picture of a cancer that can be taken as a guide. In probably 90 per cent of the cases there is no difficulty. This percentage however is getting less and less, and, *vice versa*, our problem is getting greater and greater. Without a doubt this is due to the increased interest manifested by the laity and profession in the ferreting out of suspicious lumps with which the human frame seems to be so frequently cursed. The 10 per cent represents our difficulties. Inadequate amounts of the tumour tissue sent in for examination, or insufficient history accompanying it, keep this percentage unnecessarily large. When these are eliminated we still have a definite percentage to worry about, and here all the skill and technique available must be brought into play.

In the final analysis there are only some three or four features revealed by the microscope upon which we have to evaluate the growth. First, the general characteristics, such as evidence of infiltration of the growth into surrounding normal tissues. This, of course, presupposes that a proper section has been taken from the growing margin. It is not, however, always apparent, even when numerous sections are taken from various areas. Many benign tumours also have this same characteristic, for example—moles, angiomas, giant-cell tumours.

Secondly, the arrangement of the tumour cells, one with another and with the surrounding stroma. To evaluate this, of course, a thorough understanding of normal physiological and inflammatory variations must be constantly kept in mind. In the 90 per cent infiltration is usually present, and is, of course, a great aid. In the 10 per cent it is very often lacking; that is, the cells all appear fairly normal in their arrangement, one with another and with surrounding stroma cells.

We are coming now to our last stand, the most important and critical, and often the only, point on which a diagnosis is made. I refer to the typical or atypical characteristics of the individual cells. Now we are not "one-cell pathologists". There are some who claim to be able to identify an individual cancer cell. Very few pathologists have the temerity to admit of such skill or even to agree that it is possible. In evaluating the divergence from normal to cancer cells, I believe judgment passed upon one cell is quite unsound. The whole picture with many fields must be studied under the microscope. If doubt still exists, more blocks should be put through; it is surprising how this latter simple procedure so often clears up the obscurity of the first blocks and makes the diagnosis comparatively easy. These atypical features of cancer cells are sometimes quite obvious to the trained eye. At other times the variation from normal is so slight that one forms his opinion almost by intuition: it may be just a little increased density or intensity of staining of the nuclei; a prominence of the nucleoli; a variation in the size of the cells; or a disproportion in the volume of cytoplasm as compared with that of the nucleus, that one feels is not normal. I mention these points to show you that the diagnosing of cancer is not an exact science, that it is not governed by any known

set of rules. It is really an opinion given by the pathologist based upon certain evidence as revealed by the gross and microscopic appearances.

I feel that the clinician up to a certain point can diagnose with confidence and certainty a definite percentage of malignant tumour growths that come to his attention. There may lurk however in his mind the element of doubt, and he may feel a desire for confirmation before he takes a radical step which may involve the patient in needless expense or danger of life. The same might be said for the radiologist. Now I am not trying to belittle their skill, for in many cases I know one can quite confidently take their opinions as final. However, whether for confirmation or diagnosis, all tumours, I believe, should be brought to the attention of the pathologist. Depending upon his skill and experience his diagnosis can be accepted with confidence in the vast majority of cases. He is equipped to reach more nearly the ideal of a perfect diagnosis than probably any other branch of medicine. I have left room, however, for the human error to creep in. This is the privilege of *Homo sapiens* living under the stress of modern civilization. Such a state, however, is not ideal. I believe that it can be consider-

ably improved. New knowledge comes by experience and experiment. In our routine work we have little time for experiment, but we do have splendid opportunities for experience. This latter can be tremendously enhanced by an increase in volume of the material for study purposes and the improvement of facilities for keeping records, particularly follow-up records. These are of immense value and enable one constantly to repair and reinforce the foundation upon which our whole scheme of diagnosis is built. In the unusual cases the final diagnosis should not be left with the pathologist alone, or in fact with any one person or medical division. All the forces at our command must be brought into play. Rivalry in skill must be set aside, and the problem attacked in a group manner. The clinician, radiologist, pathologist, and any others who have anything to contribute should sit down together, as it were, and form a group opinion. This is not the expression of a desire on the part of the pathologist to evade his responsibilities. It is a desire to offer something a little better for the patient and something more exact for the clinician, thus approaching more nearly to the ideal which is the goal of every true follower of Hippocrates.

## Case Reports

### PITUITARY EXTRACT IN THE TREATMENT OF ALOPECIA\*

By A. W. M. WHITE,  
*Toronto*

In 1931, Bengtson reported (*J. Am. M. Ass.*) that in the treatment of a case of Fröhlich's syndrome with anterior pituitary extract, a luxuriant growth of hair took place. This experience led him to treat in the same way a number of cases of alopecia uncomplicated by other signs of endocrine imbalance, and the reports of these cases showed surprisingly satisfactory results.

I wish now to report one case of alopecia totalis which has been under treatment for

eleven months. The treatment was undertaken at the earnest request of the patient who begged that something be done. The patient is a spinster of 73 years, who has always been healthy and has worked at dressmaking for almost 60 years. Generally speaking, there is nothing abnormal about her development, and she has made a success of her work all her life.

She stated that until she was 31 years of age she had beautiful hair, which was long and thick. At that time she noticed a small area the size of a twenty-five cent piece on the top of the head that was quite bald. This area gradually increased in size until within six weeks her hair had entirely disappeared. Within another few weeks the eyebrows, lashes and axillary and pubic hair was lost. She resorted to every type of treatment of which she heard, but without result. At times, usually about twice a year, there has appeared a fine fringe

\* Read before the Section of Medicine, Academy of Medicine, Toronto, on March 13, 1934.

of lanugo, about one and a half inches wide around the sides and back of the head. This was a very fine, downy growth, never more than a quarter of an inch long, which always disappeared after two or three weeks.

The past history was that she had always been healthy, with the exception of an attack of rheumatic fever at the age of 16, which kept her in bed for 6 months. The family history is interesting in that she had one sister who lost her hair at 3 years of age. It grew again, and came out a second time at 28. Again it grew, but was lost permanently at 45 years. One nephew, now aged 43, has had alopecia totalis for 16 years.

The routine physical examination showed nothing abnormal, except a mild degree of chronic arthritis of the shoulders and small joints of the hands. There was a complete absence of hair on any part of the body. The skin itself presented nothing worthy of note. The Wassermann test was negative.

Treatment was begun on April 15, 1933, with a saline extract of anterior lobe of pituitary gland, furnished by the Eli Lilly Company. She was given 1 c.c. hypodermically three times weekly.

At examination on July 10, 1933, after three months' treatment, the whole scalp, with the exception of three small areas about one inch in diameter on the top of the head, was covered with a fine growth of hair about one-quarter of an inch long. This hair had a definite wiry quality, and the patient was satisfied it was of a much coarser character than any of the sporadic growths of lanugo. Around the base of the occiput the growth, while present, was somewhat scanty.

On November 15th, seven months after beginning treatment, there was a definite growth of hair over all parts of the scalp that had shown some growth in July. The hair was about 2½ to 3 inches in length and definitely wiry. The three small bald spots on the top of the head remained, and the growth under the occiput was still quite thin.

The treatment has been continued and the hair has continued to grow in length, and in the last few weeks a number of hairs in the eyebrows and some fine eyelashes have appeared.

I do not wish to draw any conclusions from this one case, but merely present it for the interest it holds.

## A VASELINE BOTTLE IN THE RECTUM

By W. F. GILLESPIE, M.A., M.B.,  
F.R.C.S.(C.), M.S.,

*Department of Surgery, University Hospital,  
Edmonton*

No. 13930, A.G., a sixty-four year old Irish peddler was admitted on May 6, 1932, with the history of having inadvertently allowed a vaseline bottle to slip up the rectum twenty-four hours previously, when trying to relieve an exacerbation of pain from his piles and constipation. The remainder of his history was essentially negative.

Examination showed a rugged Irishman, apparently in good health. The anal orifice was somewhat dilated and markedly congested, with some ecchymosis under the perianal skin. There was no apparent laceration of the muco-cutaneous line, but there was a moderate flow of blood from above the sphincter. Digital examination revealed the butt of a large vaseline bottle which receded from the finger.

He was given an anaesthetic, but all attempts at manual version failed. After several instrumental failures, a Braun's hook was inserted past the bottle, whose neck it engaged on withdrawal, and removal was accomplished. Two lacerations were caused by this manœuvre, one on the right, twelve centimetres long and quite deep, the other on the left being shorter and shallower. The former was closed with five interrupted plain catgut sutures. A silk pack with tapes was inserted into the rectum and a similar one was placed in the nates with the tapes of the former tied snugly over it.

His post-operative course was uneventful and he escaped peri-rectal suppuration. The pack was removed in twenty-four hours, and he received two rectal acriflavine irrigations daily. At the end of the week he was discharged (May 14, 1932) and was kept under observation for a month.

## AN INK BOTTLE IN THE RECTUM

By H. GURTH PRETTY, M.D.,  
*Montreal*

On the morning of May 23rd, F.C., a male, aged 40, had an ingenious idea of applying heat to the prostate by filling a 4-ounce fountain-pen

ink-bottle with hot water. The water was poured out, and the mouth of the bottle was inserted into the rectum. There was gradual dilatation of the anal sphincter, when, suddenly, there was a pop and the entire bottle disappeared. The patient was much concerned and attempted to remove the bottle, first with his fingers, and then with two hooked pieces of wire, which he passed up the rectum with the hope of grappling the neck of the bottle. He was unsuccessful, and within an hour of the disappearance of the ink-bottle presented himself at the hospital.

*Local condition.*—The anal orifice was somewhat dilated, and through it blood and mucus were escaping. A gloved finger was inserted into the rectum, which immediately confirmed the story. The words "made in Canada" could be felt and read on the base of the bottle! On account of the amount of trauma to the sphincter, and the possibility of perforation of the rectal wall by the wire I immediately admitted the patient for extraction of the foreign body. He began to suffer severe cramping, bearing-down pains. These were controlled by morphine sulphate, gr.  $\frac{1}{4}$ .

*Operation.*—The patient was given a low spinal anaesthetic with stovaine, and immediately put up in the lithotomy position. The anal sphincter was then gradually dilated. It was not necessary to incise the sphincter. The base of the ink-bottle could be clearly seen, situated above and between the base of the prostate and the tuber ischii. Many attempts were made to extract the ink-bottle with the aid of spatulae and various types of forceps, and also by passing sterile tape around the neck. The bottle, however, just swung around like a cyst on a pedicle. The idea was then conceived that the only way to extract it was to overcome the vacuum. An attempt was first made to liberate the mucosa from the mouth of the

bottle. This however, was not possible. The next idea was to make a hole by means of fusing a cross in the base of the bottle with the electric cautery, immediately chilling the glass with a wet swab. When finally the cross was almost fused through the base of the bottle, a gentle tap with a sharp-pointed instrument produced a transverse fracture. Half of the base of the bottle and part of the wall was then removed with forceps, great care being taken not to lacerate the bowel wall. This having been done, an attempt was made to remove the remainder of the bottle. This was impossible, since the mucosa and the bowel wall had herniated into the neck of the bottle, and had then mushroomed themselves inside as the result of oedema. The remainder of the bottle was then removed piecemeal, after being broken with bone-cutting forceps. It was impossible to remove the neck of the bottle without fracturing it. When all the particles were removed, the rectum was carefully examined digitally, and when all particles of glass had been removed, it was swabbed out with wet gauze. A speculum was then inserted and the anal canal and rectum packed with acriflavine emulsion gauze. There was surprisingly little bleeding. The patient was sent back to the ward, put up in a high Fowler's position, and the blood pressure and pulse recorded every half-hour for the following 6 hours. During that period he was watched for profuse haemorrhage and the onset of peritonitis. He was allowed clear fluids by the mouth for 48 hours, pil. opii., gr. 1, t.i.d., and morphia, gr. 1/6, for pain and peristalsis. The gauze drain was removed, and the patient given two one-ounce doses of liquid paraffin and soft diet. The remainder of the convalescence was uneventful.

This case is of interest, since the foreign body was extracted successfully without opening the peritoneum by the abdominal route, as is frequently necessary under such conditions.

**METHYLENE BLUE: A SYNERGIST, NOT AN ANTIDOTE, FOR CARBON MONOXIDE.**—H. W. Haggard and L. A. Greenberg state that there is no valid basis, theoretical, experimental or clinical, for the belief that methylene blue is an antidote for carbon monoxide asphyxia. The chief effect of methylene blue is to convert some of the haemoglobin of the blood into methaemoglobin. By thus further diminishing the oxygen-carrying capacity of the blood, methylene blue acts as a synergist with carbon monoxide in promoting asphyxia. It probably exerts

also other deleterious effects. The authors present experimental evidence showing that the administration of methylene blue in carbon monoxide asphyxia may induce fatalities that would not otherwise occur. Illness attributable to the effects of methylene blue persists after recovery from carbon monoxide asphyxia. These conclusions reinforce previous evidence that hypodermic and intravenous medication is more likely to be injurious than remedial in the treatment of carbon monoxide asphyxia.—*J. Am. M. Ass.*, 1933, **100**: 2001.

## Editorial

### RECENT STUDIES ON SILICOSIS

SILICON, in its many combinations and derivatives, is one of the most widely distributed elements in nature. It is found in many rocks and minerals, in most food-stuffs, particularly those of vegetable origin, and in nearly all dust. Consequently, it is constantly entering the animal body, and, to some extent, therefore, may be regarded as a normal constituent thereof. It has definitely been shown that silica in solution can exert a toxic action on the tissues. For example, it can produce coagulation necrosis of cells, fatty degeneration of the heart muscle, and necrosis of the liver parenchyma. That it does not produce harmful effects more often is perhaps linked up with the fact that it is readily excreted, the renal threshold for silica being low, as King, Stantial and Dolan<sup>1</sup> have proved. The dosage, also, would naturally have to be taken into account here. At any rate, so far as our present information goes, there is only one situation in the human body where the presence of silica is associated with pathological change, namely, the lung. The peculiar, and apparently specific, lesions in this organ attributed to silica are due to the inhalation of dust over prolonged periods, and are particularly related to certain occupations, such as mining, stone-cutting, sand-blasting, tool, axe, glass, slate, porcelain and silica grinding, moulding, vitreous enamel spraying, and abrasive soap manufacturing. Rarely, silicosis may develop where we would not suspect it, as in cotton-carders and in those engaged in polishing the heels of boots.

The chronic lesions produced in the lung by the inhalation of dust have been grouped in the past under the term "pneumonokoniosis," and a variety of this, due to silicon, was known as "silicosis." The Committee on Pneumonokoniosis of the Industrial Sec-

tion of the American Public Health Association recently defined silicosis as

"a disease due to breathing air containing silica ( $\text{SiO}_2$ ), characterized anatomically by generalized fibrotic changes and the development of miliary nodulation in both lungs, and clinically by shortness of breath, decreased chest expansion, lessened capacity for work, absence of fever, increased susceptibility to tuberculosis (some or all of which symptoms may be present), and by characteristic x-ray findings."

This definition, which, as a matter of fact, is a description rather than a definition, by intention excludes disease produced by other kinds of dust, such as coal, asbestos, and talc dust. It is questionable if this is justifiable. For purposes of workmen's compensation silicosis is defined in Ontario more briefly as "fibrosis of the lungs due to the inhalation of silica dust."

The pathogenesis of silicosis may be epitomized as follows. The affection begins as a dry bronchiolitis. Dust-laden phagocytes accumulate in and about the intrapulmonary lymphoid tissue and pass into the lymphatics of the lung, eventually reaching the tracheo-bronchial lymph-nodes. Fibrous tissue gradually develops within these aggregations of phagocytes and characteristic laminated, hyaline, fibrous nodules are produced which ultimately undergo degeneration. These nodules gradually enlarge by extension at their periphery, so that further areas of pulmonary tissue become involved. It may prove to be the case, however, that the first manifestations of silicosis occur in the tracheo-bronchial lymph-nodes. The sequence of events is important.

Silicosis presents certain peculiar features, is a deadly disease, and constitutes in many countries a serious industrial hazard, so that it is not surprising that it has attracted widespread attention in recent years. Much good work has been done in Great Britain, South Africa, Canada, and the United States, partly in elucidating its pathogenesis and pathology, and partly in devising preventive

1. KING, E. J. AND STANTIAL, H.: Biochemistry of silicie acid, *Biochem. J.*, 1933, **27**: 990.

KING, E. J., STANTIAL, H. AND DOLAN, M.: Biochemistry of silicie acid, *ibid.*, 1933, **27**: 1002, 1007.

measures. In this connection we might cite certain papers emanating from the Banting Institute, Toronto, the most recent of which have been appearing in our *Journal*.<sup>2</sup> But despite intensive study many important points remain unsettled. We may ask, here, several questions. Is silicosis merely one form of pneumonokoniosis, or is all pneumonokoniosis silicosis? Is the agent which produces such serious changes in the lung silica, some other derivative of silicon, or a combination of substances, some siliceous and some not? What is the relationship between pulmonary tuberculosis and silicosis? What is the most efficient method of prevention?

From the pathologist's point of view it can be at once stated that there is room for the generic term "pneumonokoniosis", to cover all cases in which there is inhalation of dust with attendant tissue changes. We note that Prof. M. J. Stewart, of Leeds, adheres to the classical division of pneumonokoniosis into anthracosis, silicosis, and siderosis, and adds the recently described entity, asbestosis. As asbestos is a silicate there seems to be no very good reason for separating it from other forms of silicosis, unless, indeed, on the basis of a somewhat different morbid anatomy. But, it has to be admitted that many dusts are comparatively innocuous, and, from the clinical point of view, silicosis is the all-important form of pneumonokoniosis. Naturally, many dusts are compounds of varying substances. Thus, coal-miners, notably those working with anthracite, are exposed to mixtures of carbon and silica, and haematite workers, as in west Cumberland, England, to iron and silica. Usually it is to the silicotic element ( $\text{SiO}_2$ ) to which the harmful effects in silicosis are attributed. More experimentation will be required before the relative degrees of toxicity of the various components of dust can be determined. This point has a bearing on the question of the relationship of

silicosis and tuberculosis. Some recent work of Prof. E. H. Kettle<sup>3</sup> gives promise of affording us a ready means of classifying dusts. We quote the *Lancet's* account of this study (*The Lancet*, 1934, 1: 904). "Where a noxious dust reaches the lung through inhalation or through intratracheal injection, the first lesion to be observed is in the glands at its base. As early as three months after intratracheal injection of a suspension of crystalline silica, or of finely ground flint, changes can be observed in the pulmonary glands long before true silicotic lesions in the lungs are visible; but that these ultimately develop was shown by the examination of other animals in the same series which were allowed to survive for much longer periods. Control experiments with iron-coated silica and wellingtonite, both being inert dusts, showed merely a copious deposition of dust without any cellular activity or fibrosis. Since these observations were only incidental to the main object of the experiments, which was the study of the later pulmonary lesions, the earliest date at which the changes can be found was not ascertained. But it is clear that in the short space of three months or less it should be possible to estimate whether any given dust is likely to be among the active or inert dusts, though it is not claimed that a dust can be finally incriminated on indirect observations. Application of the method on a large scale might well result not only in a definite preliminary classification of dusts but in the establishment of standards by which any samples could be tested."

Until recently it has been fairly widely accepted that silicosis is due to the accumulation of silica (silicon dioxide,  $\text{SiO}_2$ ) in the lungs. This silica does not produce its effects by mechanical irritation leading to death of phagocytes and productive fibrosis; rather, it is the silica which goes into solution that is toxic. Solution occurs through the action of alkaline substances and  $\text{CO}_2$ , both of which, of course, can be found in the lymph and blood plasma of the lung, as elsewhere. This explanation is now doubted by some. W. R. Jones<sup>4</sup> believes that a compound silicate—sericite—is the true cause of

2. KING, E. J. AND DOLAN, M.: Silicosis and the metabolism of silica, *Canad. M. Ass. J.*, 1934, 31: 21.  
IRWIN, D. A.: The histological demonstration of siliceous material by microincineration, *ibid.*, 1934, 31: 135.

IRWIN, D. A.: Microincineration as an aid in the diagnosis of silicosis, *ibid.*, 1934, 31: 140.  
ROBSON, W. D., IRWIN, D. A. AND KING, E. J.: Experimental silicosis, quartz, sericite, and irritating gases, *ibid.*, 1934, 31: 237.

FRANKS, W. R.: Silica dust, *ibid.*, 1934, 31: 245.

3. KETTLE, E. H.: The detection of dangerous dusts, *The Lancet*, 1934, 1: 889.

4. JONES, W. R.: Silicotic lungs; minerals they contain, *J. of Hygiene*, 1933, 33: 307.

silicosis. In this he is supported by Lyle Cummins, of Cardiff. Sericite belongs to the mica group and is a modification of muscovite, which is a hydrated potassium-aluminium silicate, but with varying amounts of  $\text{SiO}_2$  in the molecule. It is somewhat fibrous, like asbestos, which can also produce fibrotic changes in the lungs. Jones' view is supported by the peculiar fact that silicosis is very frequent in the gold-miners of the Transvaal and rare in the Kolar gold-miners of India though much quartz dust is produced in the workings in both places. Similar differences in the distribution and frequency of silicosis have been noted also in Scotland, Wales and elsewhere. Prof. Lyle Cummins<sup>5</sup> and Dr. Sladden think that Dr. Jones has made out a very good case in regard to the etiology of silicosis, and that his views, if confirmed, will explain many points now obscure in connection with the etiology of the disease. The point is being enquired into in various places at the present time, but cannot be considered as settled. The Canadian workers, Robson, Irwin, and King,<sup>6</sup> do not find that sericite plays the leading rôle. These last mentioned observers have also (*loc. cit.*) investigated the part played by irritating gases, such as are produced in blasting, in the production of silicosis. They have found that when  $\text{NO}_2$  and  $\text{SO}_2$  are inhaled by the experimental animals degenerative lesions in the lungs and pneumonitis resulted. When these gases were inhaled together with silica dust a rapidly developing (acute) silicosis was produced.

It has long been known that silicosis and pulmonary tuberculosis were apt to be associated, to a degree that could not be attributed to coincidence. A large proportion of silicotic miners die of tuberculosis. On the other hand, coal miners, even if silicotic, tend to escape tuberculosis. Various theories have been advanced to explain this. One is that mechanical injury, by destroying many of the phagocytes in the lung lessens the resistance of the pulmonary tissues and

so favours the spread of infection. This can hardly be substantiated, for the theory would apply equally well to cases of anthracosis, in which, as we have stated, tuberculosis is not a common concomitant. Another theory is that silica in solution exerts a toxic and depressing influence on the cells, and, moreover, actually promotes the growth and activity of the tubercle bacillus. Prof. E. H. Kettle, in particular has investigated this question.<sup>7</sup> He introduced into experimental animals, intratracheally, suspensions of various kinds of dust, with and without the addition of tubercle bacilli. Using an emulsion of killed tubercle bacilli, so as to mitigate the reaction, he found that when he introduced these with the active dusts the fibrotic process was accelerated, while the inert dusts remained quiescent in the pulmonary tissues or were gradually phagocytosed. He has found analogous results when the materials employed were injected subcutaneously. Experiments have also been made by other observers to determine the effect of adding silica to culture media on the growth of the tubercle bacillus. Some report an acceleration of growth under these conditions, but at the moment the findings require further confirmation and are not convincing.

In determining the relative rôles played by silica and the tubercle bacillus, it would seem desirable to determine, if possible, which condition comes first, tuberculosis or silicosis. This may be important. Bellander<sup>8</sup> has advanced the idea that if tuberculosis has been in existence first a certain degree of silicosis may be, perhaps, of as much therapeutic value as a pneumothorax. Yet, though silicosis, by hastening cicatrization about a tuberculous focus, may delay the spread of the tuberculosis, the action of tuberculosis on previously existing silicosis is quite another matter. Attempts should be made to see if there is anything in this.

A.G.N.

5. CUMMINS, L. AND SLADDEN, A. F.: Letter in *Brit. M. J.*, 1934, 1: 554.

6. ROBSON, W. D., IRWIN, D. A. AND KING, E. J.: Experimental silicosis; quartz, sericite, and irritating gases, *Canad. M. Ass. J.*, 1934, 31:

7. KETTLE, E. H.: Experimental pneumoconiosis; infective silicatosis, *J. Path. & Bact.*, 1934, 38: 201.

8. BELLANDER, J.: Silicosis in workers engaged in metal polishing and relation to tuberculosis, *Hygiea*, 1933, 95: 655.

## THE INFLUENCE OF THE HYPOPHYSIS IN HYPERTENSION

IT is now being widely recognized, though perhaps not as fully as it should be, that hypertension is not necessarily caused by arteriosclerosis, nor, indeed, that sclerosis necessarily even accompanies it. Particular stress has been in the past laid on sclerosis of the renal arterial system as being a causative factor of heightened pressure, but now we know that this relationship of cause and effect must be reversed. The sclerosis follows the rise in pressure. What causes the rise in the first instance is still obscure to us.

Dr. Harvey Cushing has recently brought forward a fresh theory regarding this unknown factor.<sup>1</sup> In brief, he suggests that the hypophysis, through its posterior lobe, plays a fundamental part in causing hypertension. He has been impressed by the fact that in an appreciable number of cases of hypertension the posterior lobe of the hypophysis shows a marked invasion by cells containing basophilic granules. He asks therefore whether it may not be possible that this basophilic infiltration is the factor activating the gland to produce its pressor substances which cause hypertension and its long train of consequences. It has of course been known for many years that such a pressor substance is contained in the posterior lobe. That it is produced by the degeneration of certain cells which break down into hyaline-like masses has been observed in animals experimentally. It is Dr. Cushing's idea to link up the excess of abnormal cellular constituents (basophils) in the posterior lobe in man with hypertensive conditions. He quotes Cannon's experiments to show that the adrenal medulla may be quickly activated,

and it is reasonable to suppose that the hypophysis may be equally responsive: "in the case of the adrenal glands, however, we do not yet know just where to look microscopically for the cytological source of the pressor principle, whereas in the neurohypophysis we apparently now do."

If this theory is correct, then the posterior lobe should show basophilic infiltration in proportion to the degree of hypertensive disorders such as eclampsia and essential hypertension, with some relation also to the arteriosclerosis and hypertension of old age. Dr. Cushing's studies on a limited series of cases do lend support to this contention, but the series is not large. In six out of nine pituitary bodies from fatal cases of eclampsia a heavy infiltration of basophilic elements has been found in the posterior lobe, and the same condition has been seen in a number of glands from cases of essential hypertension and nephro-vascular disease. As additional evidence there is the fact that such infiltration is known to be common in old age. It has so far been regarded merely as a concomitant of that stage of life, but it is at least significant that then there should also be such a tendency to arteriosclerosis and hypertension. On the other hand, it is to be noted that such basophilic infiltration has been observed in the pituitary without any accompanying hypertension or arteriosclerosis.

Dr. Cushing, as we read him, by no means feels that he has solved the problem of what causes essential hypertension, but his suggestion regarding the part played by the hypophysis, and the train of observation by which he had been led up to his idea, will certainly be a stimulus to further investigation.

H.E.M.

## Editorial Comments

### The Reorganization of our Association

Nineteen hundred and twenty-one was a critical year in the history of our Association. Debt was alarming, organization was defective, and a spirit of pessimism was rife. A Committee on Reorganization had been appointed at the Vancouver Meeting the year before, which Committee laid down certain general principles which seemed to it to be of paramount importance. It was recommended that,

to be strong, our Canadian Association should work along the lines of the American Medical Association; a much increased membership must be sought for; and the official journal of the Association must be made truly Dominion-wide in scope and influence. At the Halifax meeting in 1921 the final report of this Committee was presented, which detailed the responsibilities of the Provincial Associations towards the Dominion Association, and also the

1. Hyperactivation of the Neurohypophysis as the Pathological Basis of Eclampsia and other Hypertensive States, *Am. J. Path.*, 1934, **10**: 145.

obligations of the national body to its members (see *Canad. M. Ass. J.*, 1921, 11: 689 *et seq.*). This report will, even now, repay perusal, as indicating the wise pre-vision of its members, and, in retrospect, the degree of progress made by our Association in the succeeding years. All that the Committee adumbrated at that time has been adopted, clarified, and extended, until now we have a most efficient organization. Three points stood out at the time as of prime importance—the imperative necessity of liquidating the Association debt, the establishment of a whole-time paid Secretariat, and the development of the *Journal* to the highest possible state of efficiency. To meet the first requirement it was decided to float a bond issue among the members for the sum of \$20,000, the bonds to be of the denomination of \$100.00 each, bearing interest at 5 per cent per annum for a term of ten years. An immediate appeal was made to the members present and some fifty of them at once responded to the call. A Committee was also appointed, representing the various provinces, to implement this action. The final result was most gratifying. The sum of \$15,800 was raised, 154 bonds being issued to members, 2 to a medical and surgical clinic and 2 to a Provincial Medical Association. Four bonds were not taken up. Those who subscribed must have done so with some little doubt as to the outcome, but that their faith was not misplaced is shown by the fact that the bonds were gradually retired, beginning in 1923, until the last was redeemed in 1928. The interest was faithfully paid. The gentlemen who took up these bonds were in a very real sense the saviours of our Association. They deserve our gratitude. Their names are preserved forever in our archives.

A General Secretary was appointed in the person of Dr. T. C. Routley, whose foresight, organizing ability, activity, and tact are accountable for much of our subsequent success. The wisdom of the idea and of the selection has been abundantly justified.

The conduct of the *Journal* was reorganized, a representative Editorial Board, with collaborators and provincial editorial committees, being established, and under the able editorship of Dr. A. D. Blackader the *Journal* began a new era of progress. It may truly be said that the *Canadian Medical Association Journal* is Dominion-wide in scope, and is endeavouring to live up to the ideals laid down for it by the Reorganization Committee. A.G.N.

#### Canada and the Traffic in Narcotic Drugs

The Report of the Narcotic Division of the Department of Pensions and National Health for the fiscal year ended March 31, 1933, has recently come to hand. It is satisfactory to note that it is the considered opinion of the Department that addiction to narcotics is not

on the increase in Canada. As compared with five years ago, the situation has greatly improved. The policy of imposing long periods of incarceration upon illicit traffickers has, apparently, had a beneficial effect. Not only have many flagrant offenders been removed from their sphere of operations but their fate has, undoubtedly, proved a deterrent to some others at least. The International Convention controlling and limiting the manufacture of narcotic drugs, which was signed at Geneva in July, 1931, became operative internationally on July 9, 1933, that is, about three months after the Report under review is dated. Therefore its full effects could not be appraised at the time the report was prepared, nor, indeed, could they have been apparent. Nevertheless, some improvement had already been seen, and the Report expresses the opinion, which is well-founded, that this Convention will prove a powerful aid to the cause of the control of narcotics by rendering it more difficult to obtain illicit supplies in large quantities.

During the judicial year ending September 30, 1932, the total number of convictions under the Opium and Narcotic Drug Act was 340, as compared with 333 in the preceding year, and with 458 and 567 in the two immediately preceding years. Convictions in connection with the illegal possession, importation or selling of narcotics, however, decreased to 189, as compared with 221 in the preceding year, while those relating to smoking opium or frequenting opium dens increased to 147, as compared with 115. Why this is the case we need not speculate, as, no doubt, a number of factors, to us unknown, enter into the problem.

It is worthy of note that for the first time seizures of *Cannabis sativa* were made. This drug, which is closely allied to "hashish", is put up in the form of cigarettes, commonly known as "marijuana". According to recent information the use of these cigarettes has increased to a considerable extent in the United States and is now extending to Canada. This new menace is particularly formidable, in as much as the cigarettes are chiefly sold in dance halls and cabarets where young people not previously addicted to narcotics are apt to congregate. It is said that as much as \$1.25 each is charged for these "smokes".

The Report comments favourably on the very large measure of cooperation which is being given both by physicians and retail druggists, who seem to be alive to their responsibilities. In only one case was it found necessary to institute proceedings against a physician whose actions were obviously illicit, which actions resulted in a jail sentence. Although it may never be possible to stamp out the illicit traffic in narcotic drugs, yet the situation in this country has much improved, and, doubtless, will still more improve. One danger, however, should be pointed out. As the restrictions

against the manufacture and sale of narcotics are tightened up in Europe it is altogether likely that the illicit traffic in these drugs will acquire an impetus in oriental countries which will reach a target in Canada.

A.G.N.

### The Uncertainty of Dr. Robert G. Jackson's Age

We are all apt to hesitate for a moment or two in answering a question as to our age, and the hesitation is apt to become a little more pronounced each year. But when a man makes capital out of claiming an advanced age it behooves him to be a little more careful of these elusive years, especially if in his earlier days he has left here and there written statements regarding his age.

There is, or has been, for lately he has not been so much to the fore, a certain Dr. Robert G. Jackson who has been trying to impress upon an always impressionable public the value of a breakfast food called "Roman Meal". As is natural in this sort of impressionism, Dr. Jackson points to his own advanced age as proof of the virtues of this meal, the assumption being of course that he has fed heartily on it. He quite probably has fed thus; one would not want to doubt his word on that point. But that the meal has prolonged his life we are not prepared to accept without more convincing proof than his mere statement. Still less are we willing to believe that his life has been prolonged as long as he states. His public notices, as appearing in the newspapers, say that he is more than 75 years of age, which would make his birth year somewhere about 1859—we won't cavil at a year more or less. But in the course of his long life, Dr. Jackson has previously made statements regarding his age which are more modest in their claims, or, shall we say, more modern. In 1903, for example, he was admitted to the Jefferson Medical College of Philadelphia, and stated then that he was born in 1867. Later in life the hesitations of memory referred to began to appear, for in 1921, he said he was born in 1870. This information he gave to the American Medical Association for their directory, and they took it for what it was worth. But, being accurate people, they were disturbed, though probably not very much, by receiving another card from Dr. Jackson in 1933, in which he said he had been born in 1858. When asked to be more consistent in his statements, he replied that 1858 actually was his year of birth, but that as he had studied rather late in life he had foolishly tried to pass himself off among the "boys" as much younger than he really was. Presumably if his shyness keeps on wearing off

we will discover that 1858 is only another of his little attempts at keeping up with the boys. His method of estimating his age is evidently that which has been irreverently described in nautical language as "by guess and by God". It will be interesting indeed to see how many more years he discovers within himself at his next computation.

H.E.M.

### Dr. A. P. Procter

Our many readers will join with us in expressing our sincere regret at the dreadful misfortune which has come to Doctor Procter, of Vancouver, Secretary of the College of Physicians and Surgeons of British Columbia, and Chief Surgeon to the Canadian Pacific Railway. Doctor Procter was shot in his office by a conductor in the employ of the Railway who was the subject of Paget's disease, and whom Doctor Procter had, in pursuance of his duty, certified as unfit for work. The assailant then turned the revolver on himself and put a bullet through the jaw into his head; he is at the time of writing in a critical condition. We do not know the full extent of Doctor Procter's injuries, but are informed that when he was admitted to hospital he had hæmorthorax. The bullet struck him in the lower part of the chest, passing through his body and embedding itself in the wall. Dastardly things like this have happened before and, doubtless, will again, and no medical man is free from such risk. After making a brave fight for life Doctor Procter passed away on August 20th. The *Journal* desires to express its sympathy with the bereaved family. A more extended notice will appear next month.

A.G.N.

### Errata

We regret that certain errors have appeared in the reviews of two books which are to be found on page 116 of the July issue of the *Journal*. Under the heading "Intercortical Systems of the Human Cerebrum", by Joshua Rosett, Columbia University Press, New York, the last line of the review as it appears in the left hand column should be completed by the addition of the following— ". . . any of the investigators of that subject. The final chapter is principally a discussion of the general pattern of the subcortical pathways of the fissures, and an hypothesis is propounded with regard to the . . ." In the review of "Chances of Morbid Inheritance", edited by C. P. Blacker, H. K. Lewis, London, lines 8, 9, 10 and 11 should be deleted. A corrected version of the review of the former book will appear in the *Journal* forthwith.

A.G.N.

## Special Articles

### THE SEARCH FOR HEART REMEDIES

By EDWARD PODOLSKY, M.D.,  
Brooklyn, N.Y.

The earliest heart remedy of which we have any record is the sea onion or squill. It was first mentioned six hundred years before Christ, in that treasury of old Egyptian medical lore, the Ebers Papyrus. It was so highly esteemed among the ancient Egyptians that it received the symbolic designation of the "Eye of Typhon". It was their great heart remedy. The great Hippocrates learned about it from the Egyptians, and made use of it both externally and internally for various conditions. Pythagoras was acquainted with and wrote a treatise on it, and Pliny described a method of preparing vinegar of squill and the honey of squill for use in dropsy. It early won the enthusiastic support of the physicians of those early days. Dioscorides, the father of pharmacy, Galen and Celsus, the foremost Roman physicians of all times, Theophrastus, the great medical reformer of the Middle Ages, all recommended it in the treatment of heart affections. Strangely, with the passing of years, squill fell into disuse. After remaining in comparative oblivion for several hundred years it was rediscovered by G. van Swieten. Inspired by the work of van Swieten, Altorfi in 1715, and Duisberg in 1740, took as their thesis for the doctorate in medicine the curative virtues of squill. In 1772, Home, for the first time, made experimental studies on the effect of this remedy on the heart. In 1866 Fagg and Stevenson made an elaborate series of studies of its effects on the hearts of animals. Husemann in 1875 showed that the active principles contained in squill produced in general the same effects on the heart and circulation as did digitalis.

The search for active principles had begun in 1812, with Vogel, who isolated "scillitine"; this was also later confirmed by Tilloy, Landerer and Mandet. In 1831 Thomson isolated a substance from the bulb which he called "scillitite", but this was proved to be a chemically impure substance. Merck in 1879 discovered three glucosides, "scillipricine", "scillin" and "scillitoxin". A year later Jarmersted discovered "scillaine". In 1921 Stoll and Suter isolated a crystalline body which they called "scillarene" and which at the present time is regarded as the least toxic and most active of the principles.

At present squill is a valuable heart remedy in the armamentarium of the cardiologist. Its

effects are in many ways similar to those of digitalis. It has, however, an independent place in heart therapy. It is especially efficient in very slight cardiac insufficiency still refractory to digitalis; in severe cases, as a temporary substitute for digitalis; and in cases which for some reason no longer respond to digitalis. Finally, there are patients who to begin with respond poorly to digitalis and very well to squill. So far the results show that squill may be used with confidence in heart insufficiency.

The greatest heart remedy of all is digitalis. No one knows exactly who discovered this drug or when it was first used. As a matter of fact it was first used for other than its cardiotonic properties. Its first use in medicine goes back to the Anglo-Saxon period, where it is mentioned in the "Leechdoms" of the twelfth century. In those days it was called foxglove, which is derived from the Anglo-Saxon "foxes-glew", i.e., fox music, an allusion to an ancient musical instrument consisting of bells hung on an arched support. It was mentioned in the "Liber Medicinalis" of Apuleius, and in the "Vocabulary of the Names of the Plants" of the eleventh century, as "foxes glofa", while in a later vocabulary of the thirteenth century it is called "foxesglove". The ancient Welsh "Physicians of Myddfai" made frequent use of foxglove. It appears as an external remedy in a treatise of the year 1250. Fuchs described it in his "Plantarum Omnium Nomenclatura" in 1541, and gave it its present name of digitalis, in allusion to the German *Fingerhut* (finger-stall), and a year later gave it its present botanical description. He described its flowers as ranging from white to purple, and gave it the name of *Digitalis purpurea*, which it still retains, and which, as is quite obvious, is not a very accurate designation.

In the sixteenth century digitalis passed into the Herbals and was mentioned by Turner, and by Gerarde in 1597, who stated: "It doth cut and consume the thicke toughenesse of grosse and slimie flegme and naughtie humours". In 1640, Parkinson observed its value in "extenuating tough flegme or viscous humours troubling the chest", and remarked further that "There are few physicians use it and it is a manner wholly neglected". Ten years later, however, it was included in the London Pharmacopœia, which shows it had found its place in the *materia medica* of the physicians of that period. Previous to its first inclusion, Lobel mentioned that "The country people of Somersetshire employ a decoction for the cure of fever, but its operation is exceedingly violent".

Digitalis was chiefly employed in the treatment of epilepsy and as an external application for scrofula or the King's Evil as well as for wounds and ulcers of the legs. In a manuscript book of medical recipes written in 1644 the following formula is given for "An Oyntment for King's Evil", "Stamp a peck of Fox gloves in a stone mortar and add to it a pound of fresh butter and set them on a soft fire for four hours to make the oyntment". Another: "Against ye falling sickness take purple foxgloves, 2 handfuls of the leaves with 4 ounces of polipodium of the oak. Boil them in beer or ale and drink ye decoction. One that had this disease 26 years so that he fell with it 2 or 3 times in every month was so cured by ye use of this decoction that he had not a fitt for 16 months after." In the eighteenth century the great Dutch physician, Boerhaave considered foxglove to be of a "poisonous nature", and Haller observed that "six or seven spoonfuls of the decoction produced nausea and vomiting".

About the year 1775, in the County of Shropshire, lived an old woman who possessed a remedy remarkable for its power in curing dropsy. Her fame as an expert in curing this particular disorder spread far and wide, for many people had really been benefited. But her remedy, despite the fact that many attempted to learn its nature, she succeeded in keeping a secret. In the same year, a young physician, practising medicine in the Midlands, William Withering by name, was impressed by the fact that this old woman had "sometimes made cures of cases of dropsy after the more regular practitioners had failed". Dr. Withering determined to investigate and found: "The medicine was composed of twenty or more different herbs, but it was not very difficult for one conversant in these subjects to perceive that the active herb could be no other than Foxglove". That very year he began his study of this remarkable plant".

"I soon found the Foxglove to be a very powerful diuretic, and so in the Botanical Arrangements, published in the following spring (1776), I ventured to assert that the Digitalis purpurea merited more attention than modern practice bestowed upon it. . . . The more I saw of the great powers of this plant the more it seemed necessary to bring doses of it to the greatest possible greatest accuracy. . . . In the summer of 1776 I ordered a quantity of the leaves to be dried, and as it became possible to ascertain its doses it was gradually adopted by the medical practitioners in the circle of my acquaintance.

"In February, 1779, my friend, Dr. Stokes, communicated to the Medical Society of Edinburgh the results of my experiments with the Foxglove. At length in the year 1783 it appeared in the new Edinburgh Pharmacopœia, but from which, I am satisfied, it will again be very soon rejected if it should continue to be exhibited in the unrestrained manner in which it has hitherto been used in Edinburgh and in the enormous doses in which it is now directed in London."

In 1785 Withering published his thesis, "An Account of the Foxglove and some of its Medical Uses, with Practical Remarks on Dropsy, and Other Diseases", which ranks with the classics of medical literature. It gave the clinical histories of 163 of his own cases and many "Communications for Correspondents". Complete directions were given for gathering, stripping, drying and powdering the leaves. Regarding dosage he had this to say: "I give to adults one to three grains of the powder twice a day. Sometimes I give the powder alone, sometimes unite with aromatics, and sometimes form it into pills; if a liquid is preferred, I make an infusion. . . Patients were sometimes ordered to persist until the nausea came on and then to stop. But it soon appeared that the diuretic effect would often take place first, and sometimes be checked when the sickness or a purging intervened. The direction was therefore enlarged thus: "Continue the medicine until the urine flow or sickness or purging takes place." The "Account of the Foxglove" concluded with nine "Inferences", the last three being so remarkable that they are herewith reproduced.

"That the digitalis may be used with advantage in every species of dropsy, except the encysted; that it may be made subservient to the cure of diseases unconnected with dropsy; that it has power over the motion of the heart, to a degree yet unobserved in any other medicine, and that this power may be converted to salutary ends."

Thus digitalis as a heart remedy was given to the world by William Withering. Of its chemical nature nothing was known, but after the eighteenth century chemists began to evince an interest in the nature of this wonderful remedy. Thompson, in his "London Dispensary", 1811, alludes to the fact that Destouches established inorganic compounds of calcium and potassium, while Radig found potassium acetate in the plant. Thompson himself made a personal examination, establishing "a deep green resinous matter, in which its narcotic power resides". Leroyer, of Geneva, afterward gave the names of "digitaline" and "digitalia" to a material made by a circuitous chemical process, in which it is questionable whether the final product had any place in the original drug. Thompson sums it up as an "extractive mixture", adding that "the active principle of digitalis is unknown".

Strange as it may seem, so remarkable a discovery as digitalis failed to gain a firm foothold in the practice of medicine during the early days of its discovery. It was Sir James Mackenzie who in 1905 rediscovered Withering and brought his work before the medical profession and established the correctness of his teachings concerning the administration of digitalis. From now the study of digitalis began in earnest.

In spite of brilliant chemical research the

nature of digitalis remained a mystery. Attempts to determine the therapeutic value of the drug by chemical methods of assay proved disappointing. This led to the introduction of pharmacological estimations, based on the reactions of animals. Among the animals commonly used were the frog and cat. The frog test had for its object the determination of the amount of digitalis which would produce a permanent standstill in the heart's activity in one hour when injected into the ventral lymph sac, from which it is absorbed into the circulation. The frog method never proved very popular, nor was it accurate to any great extent. In 1910 another great name entered into the history of digitalis, when Hatcher introduced the cat method of digitalis standardization. By this means he determined the minimum lethal dose per kilogram of cat when he injected digitalis slowly into the femoral vein. This is the dose per kilogram of cat weight which brings the heart to a standstill. This estimates the action of digitalis directly on the mammalian heart, and is by far the most accurate. At the present time the cat unit is the accepted standard.

The last great name in the history of digitalis is that of Eggleston, who established the scientific dosage of the drug. One of the most important results of Eggleston's work was the demonstration of the necessity for using digitalis according to its activity, as determined by the cat method of Hatcher. Eggleston's study, ten years after Hatcher formulated his cat unit method, also enabled him to determine the amount of digitalis in terms of cat units per pound of body weight required to produce therapeutic and toxic effects. This led to the use of the so-called "Eggleston Body-Weight Method" of administering digitalis, in which the full therapeutic dose is calculated on the basis of one cat unit per ten pounds of body weight. By the Eggleston method, the calculated total amount is given in urgent cases in from 24 to 36 hours. One-third to one-half of the total calculated amount is given for an initial dose, and the remainder is divided into equal amounts and administered at six hour intervals. By this plan overdosage is prevented, as digitalis action becomes evident in six hours.

Another among the notable heart remedies has been strophanthus. However, because of its emetic effect, which is quite marked, and because its action is at times somewhat uncertain, its use has not been very wide. In 1869 Fraser isolated a glucoside which he named "strophanthin". Since then several forms of strophanthin have been recognized: the amorphous strophanthin extracted from *Strophanthus hispidus* and from *Strophanthus kombe*, and the crystallized strophanthin derived from one or other of these plants and also from *Strophanthus gratus*.

Strophanthus was studied anew by Fraenkel in 1906, who described with a great deal of en-

thusiasm the wonderful effects in the treatment of advanced heart failure. His results were confirmed by many investigators, but it was also shown that serious accidents and even sudden death occurred altogether too frequently, especially when the drug was given by the intravenous route. Its use was then abandoned, and many felt, as many still do, that it is a dangerous drug.

Among the cardiologists who did not lose faith in strophanthus was Vaquez, who was so impressed with the good results obtained from its use that he determined to investigate the reasons for its toxic action and to find a substance which would retain the undoubtedly high therapeutic value without the dangers demonstrated to exist in the strophanthins in general use at that time. He soon learned that the way in which strophanthin was prepared had a great deal to do with its toxicity, as well as the substance from which it came, and also that preparations were not constant either in activity or toxicity.

In 1882, Arnaud, professor of chemistry at the Natural History Museum in Paris, succeeded in isolating the active principle of *Acokanthera ouabaio*, a tree, the wood and especially the roots of which yielded an extract. This extract was made use of by the Pahouids and Somalis to poison their arrows. This active principle proved to be a glucoside. Vaquez immediately became interested in this new glucoside, and declared that this was the remedy which he sought. He found upon subsequent investigation that it possessed all of the advantages of strophanthin with none of its dangers. Arnaud, meanwhile continued his investigations, and, in the course of his researches bearing on the different kinds of strophanthins and the active principles contained therein, satisfied himself of the chemical and physical identity of the crystalline principle obtained from *Strophanthus glabra*, of Gaboon, and the one he had previously extracted from ouabaio wood. For this reason he gave the name "ouabain" to the crystalline glucoside obtained from *Strophanthus glabra*, of Gaboon, hoping in this way to distinguish it from strophanthus.

Ouabain fulfills at the present time a very important place in the treatment of heart disease. It is used with good results in acute dilatation of the heart; it is a remedy of emergency in advanced cases of heart failure, where in many instances an intravenous injection has proved a life-saver. Its most pronounced effect is on the tonus of the heart, and for this reason it is superior to digitalis in defects of the heart muscle.

Quinine, "the heart opium" as a German has fancifully named it, has been used for many years for its sedative action on the heart. It is thought that Skoda first recommended its use in heart disease. Its introduction into the treatment of disturbed heart rhythm dates back from

1914, when Wenkebach described its administration to a Dutch merchant suffering from this form of heart trouble. This man, living in, and acclimated to, the Dutch colonies, was accustomed to take quinine for malaria and other ills and found, curiously enough, that it also controlled his periodic heart attacks. This wonderful property of quinine in regulating deranged heart rhythm attracted a great deal of attention from physicians, and they tried it in many cases with good results. In 1918 Frey proposed the use of the dextro-rotary isomer of quinine, quinidine, in the form of its sulphate salt, instead of quinine itself. And quinidine sulphate came into the therapy of heart disease as the greatest regulator of abnormal heart rhythm we have ever known. It is at the present time, next to digitalis, the most valuable of our heart remedies.

The alkaloid quinidine was first isolated by Heijningen in 1849 from a substance called "chinoidin", a by-product in the preparation of quinine. He described it under the name of beta-chinin. In 1853 Pasteur prepared the same drug, perhaps in a somewhat purer form, and named it "chinidine". Hesse, in 1868, in referring to it, called it "conchinine". Quinidine was first used in malaria, and in the present century found its true place in the field of heart remedies. According to Sir Thomas Lewis, quinidine sulphate has the following specific effects on the heart: (1) it decreases the rate of the heart beat; (2) it stops abnormal heart rate and rhythm and brings about a return to the normal rhythm.

Among other heart remedies which have served usefully in time past and at present are *Cactus grandiflorus* and *Crataegus*. *Cactus grandiflorus* has been in use by the natives of Jamaica for many years as a remedy for difficult breathing, an outstanding symptom in heart failure. In Mexico it has been a favourite cardiac tonic. It received a thorough study at the hands of Dr. Scheele, a German physician, who was loud in its praise as a heart remedy, but it passed unnoticed for many years until Dr. Rubini, of Naples, wrote much concerning its virtues, and definitely placed it at the disposal of cardiologists, who use it now at times in cases of cardiac irritability. A well known physician, the late Dr. Green, of Ennis, Ireland, attained an extended reputation for the treatment of heart disorders. He was in possession of a remedy which he kept a secret, much in the same fashion as the old woman of Shropshire. Upon Dr. Green's death in 1894, his daughter revealed the fact that his famous heart remedy was a tincture of the ripe berries of *Crataegus oxyacanthus*. The first conspicuous American reference to *Crataegus* was in an article by Dr. J. G. Jennings, of Chicago, in 1896. From that time interest in this drug developed and physicians made many clinical tests

with it. It has been used with benefit in angina pectoris, cardiac hypertrophy, and mitral regurgitation. It is one of the minor heart remedies of note.

Ever since digitalis was discovered physicians had been on the outlook for other remedies with a possible digitalis action. Some have been discovered, but their action is not quite so marked as that of digitalis. Nevertheless, they have quite an important place in cardiotherapeutics. Quite a few cases which are refractory to digitalis have been found to yield to other drugs, among which is *Apocynum cannabinum*, or Canadian hemp. This plant has been used medicinally in this country for about a century, having been introduced to the profession by Knapp in 1826. He reported 19 cases in which the extract of the plant had been given to provoke vomiting, diarrhoea or sweating, with apparently a high degree of success. Knapp first recorded its action on the pulse; having taken a dose of 30 grains of the extract he noted that his pulse fell from 70 to 50 in one hour, and to 45 in two hours.

In 1904 Wood conducted a study of *Apocynum* on animals which showed the drug to exert a stimulating power on the cardio-inhibitory fibres and cause constriction of the blood vessels. In 1910, Dale and Laidlow isolated a crystalline active principle, "Cymarin", with which they conducted careful experiments on warm-blooded animals. They came to the conclusion that cymarin has an action which is like that of digitalis in all its respects, but is not cumulative. *Apocynum* itself brings about a quick reduction in the apex rate of the heart, a diminution of the pulse deficit, increased urinary output in all cases of oedema, and a simultaneous improvement in the general condition of the patient. But because it produces intense nausea and vomiting it has not been much used.

Another digitalis-like drug is *Convallaria majalis*, or lily-of-the-valley. This remedy has been known in medicine for several hundred years. Laigre, in 1903, refers to its use as early as 1580 by a French physician who wrote concerning it: "The Germans use it much to fortify the heart, the brain and other noble organs. They employ it also in palpitation". In 1770 the stimulating, diuretic and calming virtues of the plant in asthma and in cardiac trouble were recognized by Ferrein. Since 1880 a great majority of all articles concerning the therapeutic use of lily-of-the-valley have emphasized its truly remarkable diuretic properties, and at least one writer has pleaded for its universal adoption under the attractive caption: "Convallaria, the vegetable trocar". Two glucosides have been isolated, "convallarin" and "convallamarin". Used in heart disease the plant causes a lowering of the apex beat, an increased flow of urine, and a decrease

in such symptoms as dyspnoea, headache and other annoyances due to deficient heart action. Its action is in many respects like that of digitalis, but not so lasting. Due to the fact that it induces nausea and vomiting so readily it has not attained great prominence as a heart remedy.

Even in primitive times man seemed to realize subconsciously that a diseased tissue was often capable of furnishing its own medicine. The best results, nowadays, have been obtained in glandular deficiencies, such as that of the thyroid. Insulin, an extract from the islands of Langerhans of the pancreas, has proved, as the whole world knows, a life-saver to many diabetics. There is hardly a tissue in the human body from which an extract has not been made. The search for the hormone or hormone-like body is a magical one, and one of the most interesting attempts within recent times has established that there is a hormone capable of stimulating rhythmic contractions of the heart.

The theory that a specific hormone is elaborated for the regulation of the heart contractions was chiefly put forth by Haberlandt, a German physiologist, who in 1924 stated that he had succeeded in demonstrating a control substance formed in the sinus, a specialized bit of tissue, of the frog's heart and capable of strengthening and accelerating, on the one hand, the automatic impulse of the isolated ventricle, and, on the other, of bringing the resting heart cavity to automatic activity. He referred to this substance as the sinus hormone and demonstrated it as follows. The pulsating and bleeding sinus is plunged into a small quantity of Ringer's solution, and the upper opening of the severed ventricle is at the same time connected with a cannula. This increases the strength of the pulsation and its activity and rapidity. Ringer's solution not so passed through the heart chamber fails to give this result.

With a hormone product manufactured from beef hearts, which he later called a heart-hormone, Haberlandt undertook experiments on the frog's heart. The preparation was tested on 36 frogs' hearts, in dilutions of 1-1,000, 1-1,500, and 1-100 with Ringer's solution. With 0.5 c.c. of these dilutions the exciting, accelerating and rhythm-producing effects on the heart could be demonstrated. The pulse-exciting effects appeared in 17 experiments and the pulse-accelerating in 26, in 7 of which the automatically pulsating ventricles were first influenced chronotropically, and later in the experiment the ventricle which ceased beating was stimulated to renewed action. Such results were also recorded in 7 experiments after removal of the ventricle for a period of one day and in 3 experiments after two days' removal. It was also shown that the heart-hormone in dilutions

of 1-1,000 sensitizes the frog's heart ventricle to adrenalin. Haberlandt's experiments, though not very conclusive, were highly stimulating. His work did not show that the stimulating substance was specific. Later experiments revealed other interesting facts in regard to this.

Two other physiologists, Rigler and Singer, undertook to repeat his experiments. They succeeded in demonstrating a stimulating action on the isolated heart. They also showed that the heart muscle itself was capable of furnishing a substance which would stimulate the heart to activity. They came to the conclusion, after quite an exhaustive piece of research, that heart-stimulating substances were found not only in the various parts of the heart itself but even in organs like the spleen and liver, as well as in the lungs. These organs, when mashed up in water or in alcohol, and the heart-stimulating substance removed, had two important properties—*inotropic*, affecting the force or energy of the heart, and *chronotropic*, affecting the rhythm of the heart.

Still another German physiologist, continuing with this interesting bit of work, took various parts of the heart itself, also bits of muscle from the thigh, the intestines, stomach, and brain, and made extracts of them. These were ground to pulp with a small quantity of Locke's fluid and clean sea-sand. The mixture was extracted for about eighteen hours. Other extracts were made, using alcohol instead of Locke's solution. These were found to be effective as Haberlandt's in starting heart action. Evidently they contained a hormone, which when injected into the blood stream had a specific action on the heart in causing it to beat at a more rapid rate and with greater force.

Haberlandt was firmly convinced, as were other investigators, that the human body is capable of furnishing a definite medicine for the ailing heart, and that this was a definite substance or entity. He endeavoured to learn something regarding its physico-chemical nature. He found that the hormone remained efficacious for a long time, though in somewhat weakened measure. He also found that it was not a lipoid or fatty body. It proved to be very slowly soluble in chloroform. It could also pass quite easily through a membrane, and therefore was not of high molecular composition. It resisted heat, and this is characteristic of hormones.

He also found that his heart hormone exerted analogous, though not identical, actions on the heart as did adrenalin; while adrenalin has a constrictor action, the hormone has a vaso-dilating action. It was his belief also that the heart-hormone will make it possible to understand cardiac activity more thoroughly. More important still is that the heart-hormone could be used for clinical purposes, which is theulti-

mate aim of all laboratory experiments performed by the medical scientist.

Within the last year or so French physiologists have prepared an extract from the pancreas of the ox which they have termed "angioxyl". It has been used with particularly good success in angina pectoris. This preparation acts on the pain and helps to abolish this troublesome symptom, much to the gratification of the patient. In high blood pressure the pressure is reduced and the general condition of the patient is much improved.

The magical search for heart medicines which has been going on for so many years has borne much fruit. But there is still much to accomplish. Degenerative heart disease is still leading as the chief taker of human life, and against this form of heart disorder little can be accomplished, but now one hears something about the influence of certain vitamins on heart deficiencies. Into this interesting domain the search now leads, and what we will find here only the future can say. But the search no doubt will be an interesting one.

## Medical Economics

### ALBERTA NOTES

The Council of the College of Physicians and Surgeons of Alberta recently held a meeting in Calgary, to which were invited representatives of the different organized medical societies throughout the province. Preliminary meetings had been held by these societies during the month of July, to discuss the subjects of: (1) health insurance under the direction of the Provincial Government; (2) revision of the schedule of fees; (3) general revision of the Workmen's Compensation Board fees; (4) percentage of normal fees to be charged in municipalities for indigent work. The results of the deliberations of the societies regarding these questions were brought forward at the meeting of the Council. It was agreed that any financial arrangement between physicians and the health unit, where the health insurance scheme is being put into operation, should be backed by the Provincial Government, and should be for a stated period. It was felt that it would be most unsatisfactory to test the scheme out after having established a health unit and having agreed with the profession as to the percentage of normal fees to be paid, as all expenses would have to be paid, for the local unit district might be unable to carry out its part owing to the small amount of taxes paid, on account of general crop conditions or other factors. No health insurance scheme would be successful unless there was proper medical representation on the board which inaugurated or put the plan into effect.

It is noted that the Provincial Government was contemplating to utilize two areas for testing out the plan, but it was felt that it should

be province-wide and that it should be compulsory when put into operation. The Council endorsed the idea that there should be a free choice of physicians and that each physician should have a free choice of location and be remunerated on the basis of services rendered. It was felt that no cash benefits or compensation for loss of time through illness should be incorporated in the scheme. One point which was stressed was that whatever scheme was adopted should before adoption, be found actuarially sound. Regarding the question of fees for work done under the Workmen's Compensation Board for 1935, this subject should be considered later. A committee was appointed to investigate the question of indigent sick work and ascertain the percentage of the physicians' work, which was for the care of indigents, so that they could arrive at some fair basis of fees which might be requested from a municipality.

The Council expressed the view to the Provincial Government, some time ago, that there is a necessity of having some fund from which to pay for hospitalization and first aid medical care for persons injured in motor accidents. It was noted at the recent meeting that Great Britain has passed a law for similar purpose and gives a physician twelve shillings and six pence a mile for all distance travelled by him beyond two miles. The Council felt that it was absurd to have hospitals and physicians carry the burden any longer, as there are about one hundred thousand drivers' licenses in this province. If the fee were made an annual one it might create a fund to meet the requirements of the suggested fund.

G. E. LEARMONT

## Notes on the British Pharmacopœia and Canadian Formulary

### For the Ophthalmologist

A new class of preparations have been included in the British Pharmacopœia, which are intended to replace some of the ointments often used for application to the conjunctiva. These might well be tried by ophthalmologists, as they are said to be very superior to the old preparations. The chief difference is due to the character of the base. The old atropine, cocaine and iodoform ointments were made with lard, which did not keep well and readily became rancid, and this tendency was increased by the addition of oleic acid in the case of the two alkaloids. The oleic acid was used in order to make the alkaloid readily soluble in the lard.

The new base consists of 10 per cent of wool fat and 90 per cent of soft yellow paraffin. This, like the soft paraffin alone, which was often used in this country, will keep well and can readily be forced out of ointment tubes. The alkaloids are used in the form of their salts, and are dissolved in minute amounts of water before incorporating them with the base. Owing to the presence of the wool fat, the small amount of water will be readily taken up. The alkaloid, being in the form of the salt, is not soluble in the paraffin and will consequently readily dissolve out in the tears. It should be more readily available than the alkaloid in the old ointments, which was soluble in the base used. In part, this accounts for the lower concentration employed. These eye ointments (*Oculenta*) should be sterile, if prepared according to instructions. The list of *Oculenta* with their strength is as follows:—

- Oculentum Atropinæ: Atropine Sulphate, 0.25 per cent.
- Oculentum Atropinæ cum Hydrargyri Oxido: Atropine Sulphate, 0.125 per cent, Yellow Mercuric Oxide, 1 per cent.
- Oculentum Cocainæ: Cocaine Hydrochloride, 0.25 per cent.
- Oculentum Hydrargyri Oxidi: Yellow Mercuric Oxide, 1 per cent.
- Oculentum Hyoscinæ: Hyoscine Hydrobromide, 0.125 per cent.
- Oculentum Iodoformi: Iodoform, 4 per cent.
- Oculentum Physostigminæ: Physostigmine Salicylate, 0.125 per cent.

*Yellow Mercuric Oxide Ointment*, which was deleted from the British Pharmacopœia, is retained and available through the Canadian Formulary. It is to be noted that there are two *Oculenta* which were not paralleled amongst

the British Pharmacopœia ointments, namely those of *Hyoscine* and *Physostigmine*. *Hyoscine* has the same action as *atropine*.

*Fluorescein Solubile*.—Soluble Fluorescein is made available in the British Pharmacopœia, 1932, and if this preparation is prescribed a fluorescein of high quality should be obtained. The commercial preparations vary considerably in quality.

### The Biologically Standardized Galenicals

*Digitalis*.—The National Department of Health has made great strides in their endeavour to provide for physicians and patients in Canada digitalis in powder form and in tincture of a standardized and uniform type. Indeed, the necessary preliminary research work carried out in this field by C. W. Chapman and C. A. Morrell has attained deserved recognition by all those engaged in this problem. In the near future the preparations of all firms, as is now the case for the more important distributors, will be found to be satisfactory. The requirements in Canada should, indeed, yield more uniform products than even those of the Pharmacopœia. Both definitions require the alcoholic strength to be 70 per cent, and physicians should realize that the incorporation of tincture of digitalis in mixtures is inadvisable, since the dilution of the tincture, and particularly the presence of salts, acids and alkalies, leads to rapid loss in therapeutic strength. The safest and best flavour for Tincture of Digitalis is cinnamon, as contained in the Canadian Formulary as *Tinctura Digitalis Composita*. Even this should be freshly prepared.

The above remarks apply to Tincture of Strophanthus, though this is rarely used in Canada. The Canadian regulations require it to contain not less than 88 per cent alcohol; the British Pharmacopœia, not more than 70 per cent.

*Liquid Extract of Ergot*.—At the present moment, there is some doubt in regard to the therapeutically active principle contained in ergot, and while both Canadian and British authorities require a method of standardization which will disclose the amount of the alkaloids, ergotoxine or ergotamine, and should result in similar preparations, it remains for the future to disclose whether this method is the best test. Further, as judged by this standard, liquid preparations deteriorate rapidly, and the powdered ergot of the British Pharmacopœia appears to be the best preparation to produce definite results.

### The Biological Products of the British Pharmacopœia

We have already encountered a misconception in regard to the biological products mentioned in the British Pharmacopœia, namely, that the British Pharmacopœia description is binding in Canada. This the Canadian Formulary has already shown is not true.

The British Pharmacopœia defines Vaccine Lymph (smallpox) and Antityphoid Paratyphoid (T.A.B.) in accord with the Therapeutic Substances Act of Great Britain. In Canada, under the Food and Drugs Act and its Regulations, the first is closely defined and must be adequately tested for activity and for the presence of other organisms. In Canada, the limit for viable non-pathogenic organism is one-half that of the British Pharmacopœia. Other vaccines are not specifically defined in Canada, but are covered by rigorous regulations.

The British Pharmacopœia defines Diphtheria, Tetanus and Gas-gangrene Antitoxins and Antidysentery Serum. The first two are covered by specific regulations in Canada, while the others are covered by a general one. The Canadian regulations require not less than 350 units of diphtheria antitoxin per millilitre, the British not less than 400. In solid preparations, both require 4,000 units per gram. Again, in the case of Tetanus Antitoxin, a difference in strength is found. Nor are the definitions for Diphtheria Toxin or Toxoid and for Schick testing and Schick control identical in the two sources.

While the name adrenaline has long been included in the British Pharmacopœia, and may be freely used as a designation for this active principle in Great Britain, in Canada it is not clear as to whether this name is still a perquisite of a certain pharmaceutical house. Consequently, the word "Epinephrine" is preferred by the authorities at Ottawa, as it is in the United States, where in all medical and scientific literature the word is employed. It would be well were this example followed in Canada.

*Pituitary Extract* (posterior lobe).—Both authorities agree that the dose should always be expressed in International Units, and in Great Britain 10 units must be present in one c.c. This is not required in Canada, but is usually the case.

*Thyroid*.—The manner in which dried thyroid should be defined and standardized has not yet been finally settled, and the definitions in Canada and in the British Pharmacopœia differ considerably. Whether the therapeutic effects of the preparations conforming to the Canadian and British regulations are the same has not been determined, but there seems reason to believe that thyroid as defined in Canada is more potent than that of the British Pharmacopœia.

V.E.H. AND G.H.W.L.

### Association Notes

#### The Calgary Meeting: Proceedings of the Sections and General Sessions

The scientific program began at 9.15 a.m. on Wednesday, June 20th and was concluded on the afternoon of Friday, June 22nd. The Sections of Medicine, Surgery, Urology, Eye, Ear, Nose and Throat, Radiology, and Public Health met in the mornings. The Section of Military Medicine held a luncheon meeting on Thursday, June 21st, at the Palliser Hotel, when the medical officers who had seen overseas service were the guests of Dr. J. N. Gunn, D.S.O. On this occasion two addresses were delivered, one by Col. F. C. Bell, C.M.G., M.D., of Vancouver, on "A Special Reserve of Officers for the Canadian Army Medical Corps", and the other by Major F. C. Clarke, M.C., M.D., of Calgary, on "A Glimpse of the Past: What of the Future". The General Sessions were held in the afternoons.

Most, if not all, of the papers presented will be published in the official *Journal* of the Association during the next few months. In the meantime we are offering to our readers in this Section abstracts of such papers as have been available to us. This is an innovation which, it is hoped, will prove helpful and attractive. In the future this feature will be made more complete, and, to this end, it may be remarked, the work of the *Journal* would be greatly facilitated if those presenting papers at the Annual Meeting would be careful to prepare brief summaries dealing with the more important of their remarks and send them on to the Editor. It should be possible, then to present a complete record. This suggestion is put forth with the idea of making the *Journal* still more efficient in detailing the news of our Association. The papers abstracted below were read on June 20th and the morning of June 21st.

"Some Simple Observations and Procedures of Assistance to the General Practitioner on the Diagnosis and Eradication of Tuberculosis", was the title of a paper presented by Dr. R. G. Ferguson, of the Saskatchewan Anti-Tuberculosis League, in the Section of Medicine.

"By early diagnosis, the segregation of active cases, and the examination and early treatment of those contacts infected by these 'spreaders', tuberculosis can be controlled and the disease gradually reduced to a minor cause of death in any community."

"The sick and spreaders should be removed to a sanatorium where all facilities are available for the most specialized treatment, and where they will receive a thorough education regarding their personal habits and the technique necessary to prevent the spread of the disease."

"In the agricultural Province of Saskatchewan the fatal age period of tuberculosis reaches its maximum mortality between 28 and 30 years. The age maximum break-down from this disease in Western Canada is between 18 and 24 years. In Saskatchewan at the present

time we find that although the Indians constitute less than 2 per cent of the population they account for roughly 25 per cent of the deaths from tuberculosis. There are certain predisposing occupational hazards. The more serious of these are the dusty industrial occupations, and by far the most important among these is quartz mining of any type, where silica dust is present, especially quartz gold-mining.

"In this and in every other country the high incidence of tuberculosis among nurses is probably entirely due to infection. In 1933, 5 per cent of all patients under treatment in the sanatoria of Saskatchewan were nurses or nurses-in-training.

"Extensive examinations of family contacts in recent surveys, both in Europe and in America, have shown that the incidence of positive reactors to tuberculosis is usually two or three times as high among family contacts as it is among the average children of the community. In practice it works out that where a death occurs there are just over eight contacts requiring investigation. Since observation is required at least annually for a period of three or four years, the average family physician, after a period of five years, would have an average of forty contacts under observation."

Dr. Ferguson urged examination of the sputum of all those, young or old, who have a chronic cough. He stated that "pain in the chest has emerged as the symptom of greatest importance as an indicator of pulmonary tuberculosis."

Dr. Harold Orr, Edmonton, read a paper on "The Reactions Attending the Intravenous Use of the Arsphenamines". This is of great importance to the practitioner of medicine, because these drugs, which contain arsenic, are widely employed in the treatment of disease, notably syphilis. The administration of the arsphenamines is followed in some instances by a reaction which may endanger the life of the patient. Dr. Orr stated that "the causes of the reactions are probably as diverse as are the reactions themselves, and, though not yet fully understood, some degree of clarity is gradually emerging as a result of much intensive study by numerous investigators." He discussed the various types of reaction which may occur, and pointed out the precautions which the attending physician should take in order to prevent the appearance of an unfavourable reaction or to minimize the danger, should it appear.

Dr. W. P. Tew, of London, Ont., delivered a paper which dealt with "Recent Advances in Obstetrics and Gynaecology". In his discussion of recent advances in obstetrical practice he considered these as being of three classes: (1) those associated with pregnancy; (2) those associated with delivery of the child; and (3) those relating to the period following child-birth. The most notable recent advance first is the increasing advantage that is being taken of opportunities for pre-natal care. The regular visits made by the pregnant woman to her physician, which it is desirable to commence as early as the second month of pregnancy, give full scope for the application of preventive measures. Pre-natal care permits the physician to maintain the health of his patient through the correction of remediable physical defects, through supervision of the diet, and by the treatment of those complications which so frequently accompany the course of pregnancy. It also greatly aids the birth of a healthy child, by allowing the physician to discover at an early period those conditions which make for a difficult delivery. The recent advances associated with the birth of the child have to do with the relief of the pains of labour by the use of suitable drugs; improvements in the methods of delivery and resuscitation of the new-born child, when necessary, through use of a mixture of carbon dioxide and oxygen by means of the insufflator. The recent advances associated with the period following the birth of the child are concerned with nursing difficulties, in remedying which a high protein diet has been found of value, and in the ap-

plication of prophylactic measures against puerperal sepsis. Dr. Tew then considered recent gynaecological advances. He mentioned the progress that has been made in the treatment of menstrual disturbances, prolapse of the uterus, and cancer of the cervix. In connection with the latter, he stressed the necessity for early diagnosis if the hope for a cure is to be held out to the patient.

Dr. Wesley Bourne, Montreal, then read a paper entitled "An Estimate of the Usefulness of Some of the Newer Anæsthetics in Practice". This paper can be found in the July issue of the *Journal*, p. 44.

Drs. D. S. Macnab and E. P. Scarlett, of the Calgary Associate Clinic, in the Section of Surgery, presented a paper on "The Value of Glucose in Surgical and Medical Conditions and its Mode of Administration".

The remarkable therapeutic value of glucose in hepatic and gall bladder disease has prompted a review of certain aspects of its use in surgical and medical conditions.

In operative surgery it is important to maintain at all times an optimal glucose reserve. Pre-operatively, in most cases, this may be achieved by the oral administration of easily assimilable sugars. The use of glucose by hypodermoclysis is unsatisfactory. The ease and value of glucose administration by a vein is facilitated by the use of the continuous intravenous infusion, or so-called "continuous drip" method. The practice of giving glucose by proctoclysis was examined in detail, and the literature reviewed in this connection. The results of experiments dealing with the problem were presented. The authors concluded that glucose when given by rectal drip or massive rectal infusion in any concentration is of no value, and that its presence in the rectal solution retards the rate of water absorption.

The importance of glucose as a source of readily available energy to the heart and its value in the handling of cardiac conditions was discussed.

Finally, the value of the administration of glucose in the surgical treatment of acute abdominal conditions, and particularly in gastric surgery is emphasized. In surgery of the biliary tract it was essential that, pre-operatively, the patient receive large amounts of glucose, so that glycogen storage is secured and adequate functioning of the liver will result. Observations were set forth showing that such a procedure makes for an improved post-operative course.

Dr. Frederick W. Marlow, of Toronto, speaking on the subject of "Unusual Bleeding in Middle and Later Life", said:—"As to the necessity for a careful physical examination in cases of unusual bleeding it need only be said that any woman who does not seek to learn the cause and obtain professional advice is, notwithstanding her religious or other beliefs, a potential suicide, and that any physician, general or special, who belittles the importance of her complaint when he is consulted, or fails to make a thorough examination or advise her to consult someone who will, is a potential murderer.

"Unusual bleeding is the most outstanding feature of female pelvic disease, and often the longest neglected". Dr. Marlow went on to point out how intricate is the work of the glands of internal secretion. He likened these different organs to members of a political cabinet, each in charge of a particular service; for example, the pancreas might be designated as Minister of Fuel, Internal Combustion and Energy. Because of the interrelationship of these glands it was difficult to single out any one as responsible for menstruation. According to the speaker, "little heed has been given to what in our opinion is the most important agent in control, that is, the uterine miracle".

Dr. Marlow emphasized that there is no disease in which early recognition is more important than in cancer, and in this connection he pointed out that as unusual

bleeding is a symptom of cancer, therefore, in a case of unusual bleeding it behoves us to have in mind the possibility of cancer until a definite diagnosis is made, and that delay in establishing such may be dangerous.

Dr. F. P. Patterson, Vancouver, delivered a paper on "Acute Infective Osteomyelitis". This condition may be defined as an acute infection of a bone or bones of the body, with the production of pus. It is particularly a disease of childhood or growing adolescence. It is most serious, and if not recognized at an early stage, or if adequate treatment is not instituted, there is grave danger of fatal termination or of crippling deformities and permanent disability.

The x-ray will give a negative picture in this condition until the disease is well advanced, and it is thus necessary, as Dr. Patterson emphasized, for the physician to employ his trained clinical senses rather than depend upon laboratory aids in making his diagnosis. He stated that there is often delay in making the diagnosis because the patient does not call his physician at an early stage in the disease. It is important that parents realize that when a child has a temperature, and there is pain or tenderness in a bone near a joint, examination by the doctor is imperative. The disease often occurs in vigorous healthy children because injury sustained at play is, in many cases, the initial factor in the condition. A parent should not attempt to diagnose any such pain as rheumatism or neuritis, and should realize that the condition demands the most careful scrutiny of his doctor. Those bone infections which arise near the hip are of particular importance, because the anatomical structure in this region is such that early involvement of the hip-joint often occurs.

Dr. Patterson said that "effective treatment implies not only conservation of the life of the patient but preservation of the normal function of the limb". The treatment consists in the exposure and removal of the infected portion of the bone by surgical treatment in order that the infection may be drained and the bone given a chance to fight the infection successfully, and to produce new bone to replace that portion which has been destroyed. Dr. Patterson had found in his experience that the use of large bone grafts is a most desirable practice when the disease process has resulted in a great destruction of bone which leaves a cavity that is a source of weakness. When treatment is given early in the course of the disease the chances for a satisfactory recovery are very good. A delay in securing treatment enlarges the field of the operation, and the chance of a nearly complete return to normal is much reduced.

Dr. P. H. T. Thorlakson, Winnipeg, spoke on the subject of "Common Bile Duct Obstruction". The purpose of this paper was to show by x-rays the changes which take place in the bile ducts as the result of varying degrees of obstruction in the common duct. Five cases were quoted as the basis of the report made.

In the General Session, on the afternoon of June 20th, Sir Frederick G. Banting, of the Department of Medical Research, Banting Institute, University of Toronto, spoke on "Resistance to Experimental Tumour".

Cancer research may be said to have originated in 1889, when success attended the attempt to transplant cancer from one rat into other rats. Cancer is not a disease limited to human beings; it is found in all species of vertebrate animals. Tumours in animals may be divided into two classes—those that tend to regress and those that do not. Apparently, certain animals have a higher individual resistance to tumours than have others.

A large number of workers have used various means in an attempt to raise resistance in animals. Sir Frederick described the work he himself had conducted, stating that as a result of his experiments

certain general conclusions had been drawn. He summed up with the statement that: "At present, there is a chaos of experimental evidence with regard to the tumour problem. One must keep an open mind, in order not to confuse facts with theories. As the fundamental principles of tumour growths are the same in animals as in man, it is hoped that through animal experimentation, future research workers will provide a solution of the problem and a specific treatment for human cancer".

Prof. J. C. Meakins, Physician-in-Chief, Department of Medicine and Director of the University Clinic of the Royal Victoria Hospital, Montreal, delivered a paper on the subject of "Amœbic Dysentery in the Montreal District in 1933-34".

Dr. Meakins became interested, in the autumn of 1932, in the possibility of cases of ulcerative colitis, inflammation and ulceration of the large bowel, being due to amoebic infestation. It is the invasion of the gastrointestinal tract by the organism known as *Entamœba histolytica* which is the cause of the condition known as amoebic dysentery. This association was established for Montreal during the winter of 1932-33. In May, 1933, a systematic examination for intestinal parasites of patients admitted to the public wards of the Royal Victoria Hospital was begun, and Dr. Meakins' paper is based on the results of this work.

Forty-two cases of amoebic dysentery were discovered in 294 patients examined, and this gives a percentage of population examined of 14.3. Age and sex do not appear to affect the appearance of this disease, because the sufferers ranged from 6 months to 68 years of age, and the disease was almost equally divided between males and females. Dr. Meakins established an interesting point in that it was determined, in at least 36 of the cases that the disease must have been contracted in Canada and not in some foreign country. The present infestation is not really epidemic, but is rather endemic. That this is not a new disease to this continent is demonstrated by reference to the case-histories of proved cases of this disease during the past forty years. It is difficult to make statistical comparisons as to the frequency of this disease at the present time as compared with a number of years ago, because the condition is one which is difficult to diagnose with certainty, and many cases in the past may not have been correctly diagnosed when the present great interest in this condition did not exist.

Dr. Meakins stated that amoebic dysentery appears in three clinical forms. There is the latent case in which the causative organism is present in the gastrointestinal tract, but the patient has not, at any time, had any symptoms referable to the intestinal tract. The chronic form of amoebic dysentery is characterized by a mild and rather indefinite onset of symptoms, and it may persist for a number of years before passing into an acute condition. The acute form is characterized by a sudden and very severe onset, and, if untreated, it may terminate fatally or pass on to a chronic form. In this group of 42 cases investigated, 12 were latent cases, 11 were chronic, and 19 acute. It was found that the mortality rate was 7 per cent, and that 70 per cent of those infected have more or less severe disability. There are a number of preparations used successfully in the treatment of this condition, ipecacuanha and emetine being the best known. The treatment of the condition requires great watchfulness on the part of the attending physician, since the drugs employed may give rise to toxic effects unless most carefully supervised. Dr. Meakins stressed the need for a prolonged course of treatment in this disease in order to effect a complete cure. The reason for this is that relapses frequently occur as a result of incomplete treatment, and if a patient is discharged only apparently cured

he is a possible source of danger to other members of the community.

Dr. Meakins stated that the source of the infestation is unknown. It is believed that it is not from contamination of food. The source of the Chicago outbreak in 1933 was water and ice. It seems likely that the source of the cases in the Montreal district lies in contamination of water, ice and milk with the causative organism of the disease.

"Cancer of the Breast", was discussed by Max Cutler, of Chicago. "There is, perhaps, no organ in the body that has afforded a greater opportunity to study pre-cancerous states than the mammary gland. A mass of clinical, pathological and experimental data has been accumulated which clearly indicates that cancer in general, and cancer of the breast in particular, is not a sudden event or an accident in previously normal tissue. On the contrary, it would seem that cancer as a rule is the end-result of a series of changes which may have begun many years before. In the breast it has been possible to demonstrate a series of interrelated and consecutive changes which progress slowly over a period of many years. By the designation 'pre-cancerous' we do not mean that they inevitably become cancerous, but that they are potentially cancerous.

The well known tendency of cancer of the breast to spread early and widely renders this disease one of the most malignant of all the types of cancer with which we are familiar. The most important practical problem which confronts us is the question of early diagnosis. It is an unfortunate circumstance that cancer of the breast in its early stages is an entirely painless disease. It may reach an advanced stage without causing pain. It is because of this fact that most women fail to consult their physicians in the early stage of the disease. With the rarest exceptions, pain is not a sign of early cancer. In isolated examples, sharp, localized, persistent pain constitutes a symptom of beginning cancer of the breast. A clear, straw-coloured discharge from one or both nipples indicates changes in the breast, and such breasts should be carefully observed. A spontaneous haemorrhagic discharge from the nipple indicates a more serious condition. In the presence of a palpable tumour surgical interference becomes clearly indicated.

"The experience of most observers is that carefully performed incision of suspicious lesions of the breast for microscopical examination does not prejudice the patient's chance of cure. The indication for this procedure has increased, as an increasing number of patients consult their physicians soon after discovering an abnormality in the breast.

"It is important to appreciate that, whereas the surgical treatment of breast cancer has been standardized for many years, the radiation treatment of this disease is even today in a state of evolution. The value of radiation as an adjunct to surgery is unquestionable. The ultimate success of present efforts to replace surgical removal of the breast by radiation therapy remains for the future to determine. Until the evidence is more adequate than it is at present the radical surgical removal of the breast combined with radiation must remain the procedure of choice in all cancers of the breast which are presumably operable."

On Thursday morning "Chronic Pelvic Infection" was dealt with by Dr. John Fraser, Montreal.

Arising from conditions incidental to child-birth and other infections, it is important that there be an early diagnosis. Illhealth following on child-birth should be investigated, so that treatment may be secured promptly. Impatience on the part of the patient is noted in such cases, whereas time must be allowed if essential organs are to be restored to health. Dr. Fraser urged the importance of complete

treatment for venereal disease, so that when men marry there will be no danger of their infecting their wives.

"Bone-Marrow Efficiency", was discussed by Dr. J. D. Adamson, Winnipeg.

"The importance of the blood in the preservation of health has been recognized in all ages. Moses refers to it as the 'soul of the flesh'; Ambroise Paré called it 'the treasure of life'; and Borden says it is 'liquid flesh'. Throughout the Old and New Testaments 'life' and 'blood' are practically synonymous terms.

"Though the importance of the blood was instinctively recognized from the dawn of history, its true source remained unsuspected until men became adept in the use of the muroscope. It was Neumann, in 1868, who first suggested that the red corpuscles originated in the bone marrow. It is now almost universally accepted that all the formed elements of the blood except the lymphocytes and monocytes arise from bone marrow.

"The bone marrow is one of our most essential organs. The size of the active bone marrow is comparable to that of the liver. Modern haematology now recognizes that most so-called 'blood' diseases are more properly regarded as 'bone-marrow' diseases."

In the Surgical Section Dr. Fulton Risdon, Toronto, read a paper on "The Surgical Repair of Facial Injuries and Hare-lip and Cleft Palate Deformities". Dr. Risdon expressed the opinion that if the child is healthy successful results can be obtained in the treatment of practically all cases of hare-lip and cleft palate. Dealing with facial injuries, he pointed out that there are two stages of treatment, early and late. The object in all these cases is to correct the condition so that the patient may be able to earn his living without handicap or embarrassment due to the injury or deformity.

Dr. K. G. McKenzie, Toronto, delivered a paper on the subject of "Fracture, Dislocation and Fracture-dislocation of the Spine". He stated that, in spite of the fact that it has been recognized for many years, the normal anatomical structure is of primary importance in the treatment of fractures and dislocations, this knowledge has only been applied in recent years to cases in which there is injury to the spinal column. The reason for this is that physicians formerly feared that attempts to correct an injury to the spine by manipulation might cause injury to the spinal cord. Experience has proved such fears to be for the most part groundless, and it has been found that extensive deformities may be corrected without injury to the nervous structures. Dr. McKenzie also stated that when the spinal cord or its lower portion, the cauda equina, has been damaged in the course of the injury to the spine a striking improvement or even complete cure may result in some cases.

The speaker emphasized the importance of x-ray examination in a suspected injury to the spine, because failure to recognize and correctly treat a fracture may result in serious disability which is difficult or impossible to overcome when diagnosed at a later time. In his discussion of the treatment of fractures and dislocations of the spine, he stated that members of first aid stations should be instructed in the manner in which those suffering from such types of injury should be moved from the site, namely, by carrying the patient face downwards, so that the sagging of the body will cause hyper-extension rather than hyperflexion of the spine.

Dr. McKenzie has found in his experience that operations are rarely desirable in these injuries, and that treatment should consist of suitable manipulative procedure and fixation of the spine, i.e., by strapping

or a plaster cast when necessary. Thorough and conscientious nursing care is most necessary to ensure the full advantages from the treatment.

Dr. Gordon Fahrni, Winnipeg, spoke on "The Association of Cystic Bone-disease with increased Parathyroid Function". Hyperparathyroidism has been studied intensively since the year 1926, when a parathyroid tumour was removed for the cure of the disease. The result was so spectacular that the operation is now well established as the correct treatment.

This disease is usually characterized by pain, mild to severe, and soreness in different parts of the body. Loss of strength and weight, together with profound muscle weakness, are seen in the well developed case. Spontaneous fractures may occur.

A study of the bones by x-ray shows decalcification which may be general or local. The loss of calcium may be severe in certain parts, while other parts remain almost normal. There is usually an increase in the calcium content of the blood and a decrease in the phosphorus.

Removal of the parathyroid tumour is usually all that is necessary; the pain disappears, the blood calcium and phosphorus return to normal, and the calcium is gradually redeposited in the decalcified bones.

## Special Correspondence

### The Edinburgh Letter

(From our own Correspondent)

In last month's letter I described in some detail the nature of the evidence which has been submitted by the Scottish Committee of the British Medical Association to the Departmental Committee which is presently engaged in an exhaustive review of the health services of Scotland. In that letter I pointed out that the Scottish Committee in its Memorandum on the subject stresses the importance of the family doctor being the foundation on which any national medical service is to be built, and that in consequence it is essential that he should be efficiently trained for his work and that he should be afforded all the aids to diagnosis and treatment which modern methods require. This raises certain questions regarding the present medical curriculum. A special Committee of the British Medical Association was appointed at the beginning of last year to consider and report upon (a) the conditions that should be required for entrance upon medical studies; (b) the content of the curriculum, the position of the various subjects therein, and their proper relationship to one another; (c) the nature of examination or other tests which should be satisfied prior to graduation; (d) whether, and to what extent, post-graduate education or experience should be required prior to registration as a fully qualified medical practitioner or licence to practise independently as such.

This Committee has now issued its report,

and the changes advocated therein are directed to securing a higher standard of general education and culture on the part of the student prior to the commencement of his medical studies; a more completely coordinated course throughout the medical curriculum with a direct aim towards fitting him for the sphere of general practice; a final period of clinical responsibility under supervision prior to his complete licensure; and a considered attention throughout to the preventive aspects of medicine.

The Memorandum proceeds to point out that while an efficient family doctor service must be the basis of a good health service it is not in itself complete, and consequently certain related or adjuvant services are essential. These services consist of two groups. The first which might be called the auxiliary group, since it increases the value of the primary services, comprises consultant and specialist services. The second is the ancillary group of services, such as nursing, massage, and electro-therapy, which are administered to the patient by skilled workers under the supervision of the doctor.

With regard to the consultant and specialist service, it is pointed out that the sphere of the specialist is wide and of the greatest importance. The growth of new and highly technical knowledge in many directions has exceeded the coordinating capacity of the individual who has not made it his special study, and it is accordingly essential that the services of those practitioners who have acquired a specially high degree of knowledge and skill in relation to any particular subject should be freely available when required to supplement the services of the family doctor. There is however a popular belief that the higher attainments of knowledge and skill are only to be found in the ranks of the consultants and specialists, and it is accordingly pointed out in the Memorandum that the family doctor has had exactly the same training before graduation as all other members of the profession. It is suggested that this belief is probably due to two reasons. First, the influence of the medical schools, where it is obvious to the students that their teachers, drawn almost entirely from the consultants and specialists, have a standard and status peculiarly their own; and in the second place, the more precise and elaborate methods employed in consultant practice in hospital are constantly being contrasted in the minds of the undergraduates with the existing conditions of general practice, to the detriment of the latter. There is therefore a pull in the direction of specialization which is attracting many more of the students now than in the past in that direction, and, as has already been the case in other countries, newly qualified practitioners have a definite tendency to regard

specialization in some branch of medicine as conferring on them a higher status, and as being likely to afford them more of the amenities of life than is possible under the existing conditions of general practice. The Scottish Committee expresses the opinion that these auxiliary services should normally be mediated to the patient by the family doctor, and that the prevalent practice of direct approach to specialists by patients, both in hospital and in private practice, is not in the best interests of either party or of health policy generally.

It is recognized that if a high standard of service is to be rendered by the family doctors of the country it is necessary that the conditions under which they work should be favourable. It is stated that in many practices, especially in densely populated districts, the number of daily visits and attendances which have to be made is excessive. This renders it impossible for the practitioners to do all that they could wish for those under their charge. Their work has sometimes to be done under conditions incompatible with the reasonable needs of the practitioner for rest and leisure. Under present conditions however it is the case that many practitioners are only able to make an income sufficient to cover expenses and provide reasonably for their families by having large numbers of persons on their lists. In both these aspects, therefore, the conditions of service and remuneration call for consideration. No service can ultimately be adequate when the work has to be unduly hurried, or where the practitioner is so far fatigued that his interest in the scientific side of medicine ceases to be alert.

R. W. CRAIG.

7 Drumsheugh Gardens,  
Edinburgh.

#### The London Letter

(From our own Correspondent)

A recent statistical analysis of mortality rates at all ages revealed a very striking fact that had not been apparent before, namely, that the improved conditions at the younger ages tend to carry on for that particular generation. This makes the health of the child of even greater importance than the immediate problem of the younger members of the population. From what has been said before in these notes, despite the optimism of the reports of the school medical service, there is a strong feeling that the present period of economic depression is bound to leave a mark upon the children affected by it, even although no immediate effects upon nutrition (which in this connection means weight and height for age) are observed for the country

as a whole. Another aspect of the problem has also been revealed by the statisticians in a paper on overcrowding and health, just published by Dr. Percy Stocks. By a clever method of taking the country zone by zone according to latitude (omitting London) it is shown that the increased mortality risk well known to occur as the analysis moves northwards is associated more directly with overcrowding than with climatic factors. Overcrowding, in the sense of too many persons per room, is more important than the density of houses to the acre. The other factors commonly invoked by those who will not face the facts, such as the poverty of those dwelling in overcrowded conditions or the excuse that less fit families tend to migrate gradually into poor housing conditions, are examined and found to be insufficient to explain the variations in the mortality rates. It is especially among the age-group one to five years that the stress appears to fall, and it is here that respiratory disorders spread by droplet infection because of insufficient air-space for the inhabitants of overcrowded houses take their toll. Statistics are sometimes looked at suspiciously by medical men, but in relation to mortality rates and population problems they represent the only means of approach. At a time when the Government has promised legislation to deal with overcrowding it is particularly fortunate to have the scientific case set out in such an unanswerable manner.

Another example of a high death rate at a special age-period formed a subject for discussion at the recent National Conference on Maternity and Child Welfare held in Birmingham. It was pointed out that although in the past quarter of a century the general infantile mortality rate had fallen by one-half, the rate for the first week had only decreased by one-tenth and for the first four weeks by one-fifth. Such conditions as asphyxia, injury and prematurity appeared to account for two-thirds of these deaths, and it is yet another comment upon the problem of obstetrics whereby the maternal death rate fails to decrease despite great antenatal and other efforts that these immediate neo-natal disasters remain so high. Of those who survive the immediate hours after delivery Prof. Leonard Parsons showed that infection played the dominant part in causing death. The skin and the respiratory tract appear to be the main routes for such infection to gain entrance, modern methods having at any rate greatly abolished the risk of umbilical sepsis. Since the respiratory tract plays such an important part, even at the earliest weeks of life, as a portal of entry of sepsis it is surely a matter for great concern that those attendant upon young infants should consider acute or chronic nasal or bronchial catarrh as of comparatively trifling risk. Prof. Parsons emphasized that it is from such sources that the new-born infant gains its

fatal infection. Prevention of such tragedies would surely be a more effective way of dealing with the problem of neo-natal death than the instruction in birth control which was reported by one subsequent speaker as being among the important agencies for attacking the problem.

The British Medical Association is just concluding its annual meeting at Bournemouth as this letter is being composed. It has been complained of this meeting by the leading daily labour paper that the program contained too much about cocktail parties, manikin parades and other social activities. The volume of work done by the business side of the Association and at the Scientific Sections can safely be left as evidence against the accusation that these annual gatherings are one long riot of dissipation. The question of the recognition of chiropodists was discussed, and the Representative Meeting rejected the Council's advice to accord this form of approval and control. On the subject of abortion, which has been smouldering, so to speak, for some years, a definite decision was reached to set up a special committee to inquire into the medical aspects of this problem. The President's address was a fitting discussion of the influence of climate upon health. In view of the statistical work already mentioned, much of what is said by physicians practising in spas or health resorts has to be taken as somewhat prejudiced. This cannot be said of the Presidential address. The dangers of excessive sunshine were well stressed, and there was a good plea for rest and an adequate fluid intake as contributory factors in the maintenance of health. The whole subject was one which required scientific review and tabulation. The health resorts of this country, it was urged, were in need of necessary reorganization and improvement, much of which could be done by a healthy competition in catering and in the provision of the necessary aids to the care of invalids.

ALAN MONCRIEFF.

121 Harley St.,  
London, W.1.

Comply with same humours, bear with others, but serve none. Civil complacency consists with decent honesty: Flattery is a Juggler, and no Kin unto sincerity. But while thou mainitest the plain path, and scornest to flatter others, fall not into self-Adulation, and become not thine own Parasite. Be deaf unto thy self, and be not betrayed at home. Self-credulity, pride, and levity lead unto self-Idolatry. There is no Damocles like unto self-opinion, nor any Siren to our own fawning Conceptions. To magnify our minor things, or hug ourselves in our apparitions; to afford a credulous Ear unto the clawing suggestions of fancy; to pass our days in painted mistakes of our selves; and though we behold our own blood, to think ourselves the sons of Jupiter; are blandishments of self-love, worse than outward delusion.—Sir Thomas Browne.

## Letters, Notes and Queries

### The Department of Pensions and National Health and the Canadian Medical Association

#### To the Editor:

On reading over the memorandum and resolution objecting to the transfer of the activities of the "Division of Child Welfare" of the Department of Pensions and National Health to the "Canadian Council on Child and Family Welfare", passed at the annual meeting of the Canadian Medical Association at Calgary in June last, certain errors are noticed and it is felt that the members of the Canadian Medical Association should be fully informed of the reasons for the transfer and that the errors in the memorandum upon which the resolution is based should be pointed out.

It is regretted that the members of the executive council charged with ascertaining the facts and drawing up the resolution did not communicate with an official of the Department of Pensions and National Health before drawing up the memorandum for Council. Had they done so, certain erroneous and misleading statements would have been avoided and the necessity for the resolution might not have been indicated. There are two representatives of the Department on the Council and had they been given the opportunity of reading the memorandum before it was presented to Council they would have been in a position to make considered comments.

The framers of the memorandum have misinterpreted the duties and responsibilities placed upon the Department as outlined in the second paragraph of their memorandum. While it is true that the duty of cooperating with provincial, territorial and other health authorities with a view to conserving child life and promoting child welfare is imposed upon the Department, the method by which this is to be accomplished is not laid down. The establishment or the maintenance of a Child Welfare Division is not compulsory. The law officers of the Crown who have been consulted take this view.

In the third paragraph the following appears: "A Child Welfare Division was created in the Department in 1919. The Canadian Council on Child and Family Welfare was organized in 1922". The impression created here is that the Child Welfare Division of the Department was established two years before the Canadian Council on Child and Family Welfare, and was the parent body. As a matter of fact they were established in the same year. A Dominion Conference on Child Welfare was held in Ottawa on October 19th and 20th of that year (1920), convened by the Dominion Department of

Health, at which the Canadian Council on Child Welfare was created. The Department had agreed to call such a conference to provide for the creation of such a national body on March 23, 1920, a month after the creation of the Departmental Child Welfare Division, and a month before the appointment of its Chief.

The statement in paragraph eight, that: "The only opinions expressed so far, of which we have any knowledge, have been opposed to the action", would not have been made had the matter been discussed with an official of the Department, for there are on the departmental files numerous resolutions of a commendatory nature.

In paragraph nine, by associating the words ("since resigned") with the name of the former secretary, the impression has inadvertently been created that the resignation was made as a protest against the change; whereas, the resignation of this official was made for administrative reasons, and bears no relation to the matter in hand. It might likewise be inferred that the Chairman resigned on account of his disapproval of the new arrangement. Before the change was made he was consulted and expressed his approval, and it is believed that he has not changed his opinion.

Perhaps there is no more erroneous statement contained in the memorandum than that found in the eleventh paragraph, *viz.*, "The Dominion Government has transferred its responsibility for the conservation of child life and the promotion of child welfare . . . from a department under medical administration . . . to an organization under a non-medical director". The administration of the Child Hygiene Division of the Canadian Council on Child and Family Welfare is entrusted in addition to the full-time nursing staff, to three physicians, one of whom is a diplomate in public health, *viz.*, the Chief Executive Officer of the Department of Pensions and National Health, who acts as Chairman of the Advisory Committee; two physicians retained on a part-time basis—one in paediatrics and the other in obstetrics, and the Director of the Council who is a specialist in welfare work. The latter two physicians have regular office hours, daily, with the Council. This is clearly set forth in the memorandum effecting the transfer. These men with the other full-time staff of this Division of the Council, discuss policy, supervise the production and distribution of publications, and lecture in their respective fields.

That there should have been opposition to the move at the outset was not unexpected, as no opportunity was given the Department to state its case before such opposition was organized. It was feared by those who opposed the plan that it was the intention of the Department to completely withdraw from the field of Child and Maternal Welfare, but when it was ascertained

that the Department had actually strengthened and consolidated its position, opposition was largely withdrawn and resolutions of approval were received.

Before so important a step was taken all angles of the problem were carefully considered, and it is evident that the resolution of the Council of the Canadian Medical Association, made as it was without a full and complete study of all the attendant facts, is not justified. The participation in child welfare now exercised by the Department is technically better, clinically more expert, and the service rendered the public more effectual than heretofore. The change in procedure constitutes true leadership in the public health field, and is being increasingly recognized and accepted as such.

Yours very truly,  
R. E. WODEHOUSE,  
*Deputy Minister,*  
Ottawa,  
August 1, 1934.  
*Dept. of Pensions &  
National Health.*

## Topics of Current Interest

### The Sale of Contraceptives

In the House of Lords on February 13th Lord Dawson of Penn moved the second reading of the Contraceptives Bill, which restricts the sale, display, and advertisement of contraceptives. He said opinions on birth control and contraceptives could not be intelligibly considered one without the other. As one who had thought and written about the subject for many years, he wished at once to identify himself with the view that the way to keep the sale and use of contraceptives on sound lines was to remove the veil of doubt as to the honesty of contraception. The fact that there was a doubt as to its cleanliness and honesty prevented honest traders from taking contraceptives into their trades, and thereby the profits remained too large and the sale got into the hands of less scrupulous traders. If this slur were removed that trade would get into more normal channels. No impartial observer of events today could doubt that birth control was here to stay, and was part and parcel of our social fabric. At the same time there was good cause for protecting children and young persons from having contraceptives forced on their notice by automatic machines in streets or by lurid displays in shops. An investigation of the facts—and he had investigated facts—would show that in the main the wholesale trade was as respectably run as any other trade. The factories were well constructed; the workers belonged to a high class, and were well treated and well behaved. There was no justification for referring to the

trade as vicious. It was condemnation which sent the sale into underground channels. The same was true of propaganda. If clinics were supported which gave information which was sane, these lurid publications would cease to be profitable.

There had been a fall in the birth rate in most countries, whether Protestant or Catholic, in the Western world. If they took the years from 1880 to 1930 they would find a decline of 54 per cent in the birth rate in England and Wales, 43 per cent in Scotland, 42 per cent and 58 per cent in Catholic Belgium and Austria, and 42 per cent in Denmark. Turning to this country and this century, and taking the table of the birth rate per 1,000 married men under 55, there had been a steady fall in fecundity. That fall began among the professional classes. It was found first, for example, among ministers of religion, doctors, lawyers, and teachers. It then extended to people of other occupations, and it might now be said to have reached the artisan classes. There had been a legitimate fear that if there was a decline in fecundity in all these classes, except the classes of semi-skilled and unskilled labour, the result would be serious to the quality of the population. That would have been true if that fact had held. During one or two investigations there had recently been made a scientific inquiry into a group of wives of artisan and semi-skilled and unskilled citizens. That inquiry had had under its purview ten years—from 1923 to 1933. During that time there had been a total decline of the birth rate in the unskilled and semi-skilled classes of 14.4 per cent, and the decline was increasing, especially among the younger married men of 40 and under. What was more significant was that, if they took the gap of space between children in that class for that period of years, they found that the average gap had gone up by eight months. There was no surer evidence of birth control than a fall in the birth rate and an increase in the interval between children.

The sale of contraceptives had gone up almost by leaps and bounds. One firm at the present time turned out 8,500,000 articles a year; another firm dealing in contraceptives turned out 72,000 per week; and home production was reinforced by large importations from abroad. Contraceptives were now part of our social fabric, and to oppose them was to beat the air. No civil or military authority had ever succeeded in suppressing contraception. It had now been decided, for good or evil, that for economic and family reasons pregnancies should be limited, and that choice, not chance, should decide the size of the family. When told that these ends should be attained by self-control, young persons of today replied that they were being asked something which was new, and something which preceding generations in this

country did not practise. In effect, they were being asked to practise celibacy within the state of wedlock. In the prosperous forties of the last century the Gladstones and the Lyttones often stayed together under the same roof. In 1847, on one of those occasions, there were eleven children of the two families under 7 years of age. On another occasion there were seventeen children under 12 years. There was not much evidence of abstention in marriage there. Human nature had not changed since the forties of last century, nor had biological laws. The foundation of the home required physical love periodically repeated, yet no one would be rash enough to say in these days that families should be of equal size to those of the last century. Take a young couple who married, the man between 24 and 25 and the girl 21. They had a modest income, and properly, after the first child, or possibly the second, made up their minds that for a period of seven or eight years they would not be able to afford any more children. That could be done by abstention, which, as a medical man, he thought would be impossible, or would lead to irregularities and eccentricities, which were serious matters. In 1847 the infant death rate was 172, sufficiently high to act as a safety-valve; today the figure was down to 65. Contraception had not sprung from any evil purpose or selfish impulse; it was outrageous to say that of the young generation. Contraception was right so long as it was properly carried out, with delicacy of feeling and proper restraint.—*Brit. M. J.*, 1934, 1: 313.

#### The Depression Restoring the General Practitioner?

The economic depression has done much to restore the general practitioner of medicine, the old-time family physician, to his former eminent position, stated Dr. Dean Lewis, professor of surgery at the Johns Hopkins Medical School and president of the American Medical Association, in an address before the recent Annual Congress on Medical Education, Licensure and Hospitals. While the medical profession has been studying the problem of too many specialists within its ranks, the depression seems to have contributed not a little toward relieving the situation, in Doctor Lewis's opinion. He said that the general practitioner has actually fared better during the depression than the specialist. This is because many persons have now learned that they can be treated satisfactorily in their own homes by their family physicians.

To encourage the restoration of the general practitioner, Doctor Lewis said that conditions of life in small communities must be made more attractive. In addition, young physicians must

be trained while in the medical schools to use laboratory procedures independently, so that they will not be dependent on the equipment and consultants which can be found only in large centres. Another important factor in restoring the general practitioner to his rightful place in the medical scheme is the problem of continuing his education after he has finished medical school. Doctor Lewis suggested that a systematic plan be worked out that will take medical advances directly to the physician practising on what might be called "marginal lands". Every such physician should have contact with a hospital, he added—*The Diplomate*, 1934, 6: 85.

#### A Cheaper Process of Making Cyclopropane

Cyclopropane, an anaesthetic which is becoming popular in some hospitals because its use is not followed by nausea and also because it is relatively safe from explosion, has been prepared cheaply from certain constituents of natural gas by three Purdue University chemists, Dr. H. B. Hass, E. T. McBee, and G. E. Hinds. The process by which they have lowered its cost to a fraction of what it used to be was reported at the recent meeting of the American Chemical Society.—*The Diplomate*, 1934, 6: 170.

### Abstracts from Current Literature

#### Medicine

**Erythema Nodosum and Tuberculosis.** Ernberg, H., *Am. J. Dis. Child.*, 1933, 46: 1297.

Erythema nodosum is to be regarded as a symptom complex of a tuberculous nature, because, although no tubercle bacilli are ever found in the lesions, yet they are always associated with enlarged hilar lymph glands, cervical lymphomas of a tuberculous type, or with a phylectenular conjunctivitis. Histological sections show erythema nodosum and subcutaneous tuberculin reactions to be similar in structure. Tuberculin injected after erythema nodosum has subsided will cause a mild relapse with recurrence of the erythema nodosum. The symptom-complex of erythema nodosum may be regarded as an autogenous tuberculin reaction, thus a process of an anaphylactic or allergic nature. This unique reaction occurs under certain conditions. One of these appears to be a certain stage of the allergic condition of a system infected with tuberculosis. In many cases the erythema appears at a very early stage of tuberculosis, more particularly at the transition from the pre-allergic to the allergic stage. In some cases a certain alteration of the

allergic condition after an acute infectious disease or other circumstances may produce erythema nodosum. The erythema nodosum occurs at the same stage in a tuberculous infection as that at which the allergy becomes positive, i.e., when the patient reacts to a dose of tuberculin. This interpretation of the symptom complex of erythema nodosum has certain consequences. In the treatment one of the most important guides is the estimation of the pulmonary gland process by means of x-ray examination. Tuberculosis with erythema nodosum has in most cases a favourable prognosis. The treatment is of importance in the prognosis, and rest in bed for at least four weeks and possibly months may be necessary to avoid the possibility of miliary or meningeal tuberculosis.

The fact that erythema nodosum usually represents an early stage of the tuberculous disease makes it important to try to ascertain the source of the infection. Frequently it is possible to trace it to a formerly unknown carrier, who has perhaps neither knowledge of his disease nor understanding of its danger as a source of infection.

Finally, this conception of the pathogenesis of erythema nodosum makes it possible by means of x-ray to study and observe the development of changes in the pulmonary glands at early stages of the tuberculous disease.

GUY H. FISK

**Intra-uterine Rheumatic Heart Disease.** Kissane, R. W. and Koons, R. A., *Arch. Int. Med.*, 1934, 52: 905.

The authors review 4 cases from the literature in which rheumatic heart disease was diagnosed in infancy at the time of, or shortly after, birth. They report a case of a child who was born with active rheumatic fever and a cardiac lesion, whose mother had suffered from this disease throughout her pregnancy. The diagnosis in the child was made on the presence at birth of red, painful swollen joints and abnormal heart sounds. The joint symptoms disappeared after six months, but the child suffered from marked dyspnoea and died from heart failure at the age of nine years. An autopsy revealed rheumatic heart disease with no evidence of congenital abnormalities. The heart was greatly enlarged, especially to the right, and it had rotated in such a way that the left auricle formed the right border of the heart. They infer from this case that the intra-uterine transmission of rheumatic fever and heart disease is not only probable but possible.

LEYLAND J. ADAMS

**Sighing Respiration as a Symptom.** Baker, D., *The Lancet*, 1934, 226: 174.

The author describes a disorder of breathing which, although common, has heretofore been

almost unnoticed in symptomatology. This disorder consists of a feeling of suffocation, the end of each respiration being accompanied by a sense of effort as if working against an obstruction. This comes on at any time, especially when the subject is tired, and may last for varying periods of time, being terminated by a deep sigh after which the patients can breathe freely and easily. It affects persons without physical signs of disease, and is generally associated with a group of symptoms expressive of physical or nervous exhaustion. It is frequently described by the patients as "breathlessness", but closer inquiry will immediately differentiate it from true dyspnoea. It is of great value in assessing the part played by the nervous system in whatever condition the patient is seeking treatment for. Care should be taken to eliminate the possibility of asthma. Four cases are described illustrating the various degrees of severity of the symptom, from an occasional forced sigh to an attack lasting for hours.

Since in this condition the end of each inspiration is achieved with effort, as if against some obstruction, and since constriction of the thorax or abdomen gives rise to deepening respiration, it is believed that it is associated with a spasm of the diaphragm. The absence of any organic basis for the disorder makes the prognosis as to life good, but the symptom is often resistant to treatment and is liable to recur with the recurrence of nervous stress. It is best treated by explanation of the symptom to the patient and by eliminating any excess from his daily life. Bromides, valerian, nux vomica, and, occasionally, luminal, have all been helpful in treating cases at times.

GUY H. FISK

### Surgery

**Diverticulitis.** Edwards, H. C., *Brit. M. J.*, 1934, 1: 973.

Diverticula are bottle-necked, thin-walled sacs opening from the colon. Secondary changes depend upon retention of faecal material. Diverticulitis is commonest in the sigmoid colon since diverticula are more frequent there, and the content is solid. Inflammation may produce perforation into the peritoneal cavity, or, at the other end of the scale, chronic fibrosis of the colonic wall. This latter process may extend, i.e., perisigmoiditis, and may eventually result in obstruction. Acute inflammation added to a chronic reaction may produce localized abscesses. These may burst into a hollow organ or find their way externally. Uncomplicated diverticulitis gives a rather vague clinical syndrome. Pain, constipation, more rarely the passage of blood and mucus, frequency, and pain on micturition are the usual symptoms. Abdominal examination may reveal tenderness in the left

iliac fossa, and occasionally a lump in the same region. A clinical diagnosis should not be accepted. Radiological evidence is necessary to exclude the possibility of new growth.

The treatment of these cases consists in the avoidance of complications. Colonic lavage is insisted upon. Ordinary tapwater is probably as useful as any antiseptic solution. Two pints are used and the head of water should not exceed eighteen inches. The diet should be mainly vegetable. An excess of cellulose is to be avoided. Surgery in the treatment of diverticulitis is directed mainly at the complications. Adhesions make local excision rarely a possibility. When possible, radical procedures in the border-line cases are best. Temporary colostomy is doomed to failure. It does not allow sufficient rest to the inflamed gut. Cæcostomy gives imperfect drainage and is therefore not advisable. Permanent colostomy is necessary if the patient is to benefit. The wound should remain open for a minimum of 12 months and should be made as near as possible to the inflamed area. Operation is advisable in the interval between attacks.

One of the most dreaded complications is a colo-vesical fistula. The characteristic symptom is the passage of air and faecal material *per urethram*. Treatment is difficult. The radical one-stage operation should be abandoned. Colostomy and radical operation carries a relatively high mortality. Operation, preceded by a colostomy, should only be undertaken when the patient is comparatively young and the fistula recent. Spontaneous cure occurred in one case reported by the author.

STUART GORDON

**Perianal Tuberculosis.** Berry, F. B., *Ann. Surg.*, 1934, 99: 593.

Perianal tuberculosis may appear as (1) perirectal abscess; (2) fistula in ano; (3) soft, indolent perianal ulcer; (4) lupus; (5) submucous or subcutaneous nodular lesion; (6) or a hyperplastic type simulating neoplasm. The latter three are rare, as is a tuberculous lesion of the rectum. Tubercle bacilli reach the perirectal tissues through a diseased crypt or a local abrasion. They may occasionally arrive through the blood stream. If an abscess is formed it may appear as a typical ischio-rectal, or remain for a while as a non-tender, swelling near the muco-cutaneous margin. Eventually secondary infection occurs and the abscess breaks down. A persistent swelling with a thin profuse watery discharge from an opening surrounded by unhealthy granulations results. The external opening of a fistula is large, with purplish overhanging edges. The discharge is copious, thin and creamy. There may be multiple external openings. The internal opening is usually single. This is generally superficial or between the sphincters. In the third variety a typical tuberculous ulcer is present at the muco-cutaneous

junction. It spreads slowly either into the anal canal or outward into the subcutaneous tissue. It usually appears at the site of a pre-existing lesion, e.g., fissure or haemorrhoid.

Tuberculosis is present in only a small percentage of cases of *fistula in ano*; probably less than 10 per cent. In over 98 per cent the primary lesion is elsewhere. The incidence of tuberculosis in *fistula in ano* in patients with active pulmonary lesions is definitely increased. *Fistula in ano* may be the initial sign of tuberculosis. This disease should always be considered when a fistula appears in an underweight individual. The only proper treatment of perianal tuberculosis is excision. Secondarily infected abscesses should be widely drained. Should a tract remain it is excised. If a fistula has two or more internal openings excision should be carried out in two or more procedures. Eighteen cases are reported by the author. All were treated by excision. Thirteen were cured. Details of pre- and post-operative treatment, are given.

STUART GORDON

**Tuberculosis of the Breast.** Lee, W. E. and Floyd, W. R., *Ann. Surg.*, 1934, 99: 753.

Tuberculosis of the breast is relatively uncommon. It has been suggested that it is always due to the bovine type of tubercle bacillus. The disease is much commoner in females. It is practically always unilateral. The majority of cases occurred between the twentieth and fortieth years. The organism may reach the breast through an abrasion, through the blood stream, or by direct extension.

Pathologically, mammary tuberculosis is best classified as follows: (1) acute miliary, (2) nodular, (3) sclerosing, (4) obliterans, and (5) various atypical forms. The lesion commences in the mammary stroma. After several months a palpable mass is formed. Rarely this exceeds the size of a hen's egg. It may become encapsulated and lie quiescent for a time, or it progresses to sinus formation. The sclerosing type is a slow progressive lesion and is most frequently seen in elderly people. The breast is not enlarged; the nipple may be retracted; sinus formation is rare. Tuberculosis of the breast is sometimes associated with adenoma or carcinoma.

A painless lump in the breast is the first thing noted in 75 per cent of the cases. In the remainder either pain, a discharge from the nipple, hardening of the breast, or sinus formation constituted the first indication. The physical findings vary with the stage of the disease. The mass may have all the characteristics of carcinoma. An unruptured abscess cannot be differentiated from a simple cyst. There is axillary lymph-gland involvement in over 50 per cent.

Tuberculosis usually occurs at a younger age and runs a more acute course than carcinoma. The absolute diagnosis is made by histological demonstration of a tuberculous lesion, or the development of tuberculosis in animals following inoculation of pus or scrapings from the lesion.

There are no cases of proved breast tuberculosis in which spontaneous regression has occurred. The treatment is surgical removal. Accompanying lymph-node involvement may be dealt with surgically, or may be treated by roentgenotherapy. If untreated other organs may be attacked and death result.

The prognosis following proper treatment is excellent in primary breast tuberculosis. In cases of secondary breast tuberculosis it depends upon the degree of tuberculous involvement elsewhere.

The author reports three cases.

STUART GORDON

**Obstetrics and Gynaecology**

**Hæmorrhage in the Later Months of Pregnancy.** Hendry, W. B., *Am. J. Obst. & Gyn.*, 1934, 27: 408.

Hæmorrhage stands second only to infection and toxæmia as a cause of maternal death. Of 7,448 admissions to the Burnside Lying-in Department of the Toronto General Hospital during the last ten-year period there were 56 cases of placenta ablata, an incidence of 0.75 per cent, and 83 cases of placenta prævia, 1.11 per cent. Hendry prefers the term "placenta ablata" to that of "accidental hæmorrhage" with its suggestion of accident or injury. In the 56 cases of placenta ablata the hæmorrhage was concealed in 17, revealed in 30, and both concealed and revealed in 9 cases. Placenta ablata must be considered one of the complications of the late toxæmias, and might well be classified itself as one of the toxæmias. In 34 cases labour started spontaneously, 9 were induced by rupture of the membranes alone and 5 by the hydrostatic bag. Cesarean section was performed in 3 and subtotal hysterectomy in 5 cases. Every case of hæmorrhage from the site of a normally placed placenta, whether moderate or severe, must be viewed with suspicion, and, whether labour starts spontaneously or is induced, the possibility of severe post-partum hæmorrhage should always be kept in mind and preparation made to control it.

In 83 cases of placenta prævia the placenta was described as central in 16, marginal in 47, and lateral in 20. Age did not appear to have any bearing on the etiology of the condition, but parity seemed to have etiological significance, as there were only 7 nulliparæ in the series, 20 primiparæ and 56 multiparæ, 17 of the latter having had from 4 to 15 pregnancies

each. In 15 cases the haemorrhage was mild, in 30 moderate, and in 38 severe. Twenty-four were either in labour on admission or went into labour spontaneously shortly afterward. Labour was induced in 36 cases and Cæsarean section was performed in 23 cases. Pituitrin was used intramuscularly in 10 cases and proved to be of value in controlling haemorrhage and shortening labour.

Considering the whole series in retrospect, it appears to be in the best interest of the patients to employ such therapeutic measures as appear to be best suited to the individual cases, whether these measures are surgical or conservative, rather than to follow a cut and dried method of procedure in every case. Both the public and the profession should be constantly reminded of both the significance and the danger of uterine haemorrhage in the later months of pregnancy.

ROSS MITCHELL

**Extensive Perineal Damage at Labour.** Little, H. M., *Am. J. Obst. & Gyn.*, 1934, 27: 414.

In studying the cause of frankly complete tears involving the bowel one factor stood out, narrowing of the sub-pubic angle and shortening of the bi-ischial diameter. It is an obstetric axiom that when the bi-ischial diameter of any pelvis equals, but does not exceed, the distance between the blades of any standard forceps, then, during extraction of the head, both blades of the forceps, together with the major portion of the head must lie behind the bi-ischial line, in which event serious damage to the perineum is absolutely inevitable.

The ultimate results are for the most part excellent. Immunity from permanent fistula formation in Little's own cases was due to the fact that no catgut, save one fine strand to bring together the ends of the sphincter, was knotted in the perineum, and that approximation of tissues with non-absorbable material was invariably preferred to the use of buried catgut. After repair of the rectal mucosa, knots in the lumen of the bowel, the sphincter ends were approximated with very fine catgut, and silk-worm gut was then used to bring the torn or cut perineal body together, and also as a figure-of-eight to reinforce the fine catgut in the sphincter. Tissues should not be devitalized by too tight suturing, and the sphincter should not be anchored in the mucosa or overlying skin.

There is no danger from bowel activity after repair, unless purgatives have been administered. Opiates are absolutely unnecessary. Restriction to fluids for the first two days and to a diet with small residue for five days is no hardship. Care of the bladder is important.

Complete laceration of the perineum is essentially a matter of first deliveries. Too prolonged labour is undoubtedly a factor both in the production of damage and in the failure to heal subsequently.

ROSS MITCHELL

**Cardiac Disease in Pregnancy.** Stander, H. J., *Am. J. Obst. & Gyn.*, 1934, 27: 528.

Pregnant patients suffering from heart disease may in general be divided into three groups, although these groups are not definite and often overlap. Group I comprises those who have some history of heart disease, who show a heart lesion, either congenital or acquired, but who have not had any sign or symptom of cardiac decompensation and who are able to stand the strain of every day life without any signs of decompensation. Group II includes those who have a cardiac lesion, have no history of cardiac decompensation, but who are forced to limit their activities. Group III takes in those patients who have a definite history of cardiac decompensation.

The treatment in the first class usually consists in careful ante-natal examinations and observation, admission to the hospital a week or two before term, with spontaneous delivery under ether anaesthesia. The treatment in the second class of patient is an even closer vigilance, admission to the hospital a month or more before term, and avoidance of the second stage of labour by application of forceps on full dilatation of the cervix. In the third class the treatment should undoubtedly be radical; in general pregnancy should not be allowed to continue, and subsequent pregnancy should be prevented by sterilization.

ROSS MITCHELL

### Pathology and Experimental Medicine

**Blood Cholesterol and Hypometabolism: Suprarenal and Pituitary Deficiency, Obesity, and Miscellaneous Conditions.** Hurxthal, L. M., *Arch. Int. Med.*, 1934, 53: 825.

Since a lowered metabolic rate is sometimes found where the thyroid function is not deranged, whereas thyroid deficiency is always accompanied by hypercholesteræmia, it might be well to observe the blood cholesterol in other cases of hypometabolism.

There are a certain number of cases in which the metabolic rate is not a safe guide; others, where it does not seem directly related to the state of the thyroid. Is it possible that other endocrine glands affect the metabolic rate, that a hypometabolism without hypercholesteræmia might be unrelated to the thyroid?

The metabolism may be lowered by either thyroid, suprarenal or hypophyseal deficiency, the latter associated with chromophobe tumours. There is no doubt that the suprarenal plays a part in the causation of the hyperthyroidism picture. How important a part? On the other hand the thyroid is not deficient in Addison's disease, as hypercholesteræmia is not present.

There is, of course, an intimate relation be-

tween the pituitary and the thyroid; is the enlargement of the thyroid a reaction to the increased metabolism caused by the pituitary hormone, since the thyroid atrophies after hypophysectomy? A study of obesity cases which showed low metabolic rates without hypercholesteræmia shows they have not always a thyroid origin. Again myxœdematous patients are not all obese. Estimation of the blood cholesterol would have value in the managing of a case of obesity before launching the patient on the chartless sea of thyroid administration.

P. M. MACDONNELL

#### Diverticula of the Duodenum and Jejunum.

Edwards, H. C., *The Lancet*, 1934, 1: 169.

The author gives a fairly complete summary of the different types of diverticula that affect the duodenum and the jejunum. He gives a classification of these conditions. In his primary acquired diverticula of the duodenum he finds no muscle coat. He considers that the factors causing the diverticulae are the presence of a weak area in the muscular wall, and, secondly, a pulsion force from within the bowel. In the duodenum he feels that it is usually associated with a pylorospasm, and that what calls for operative treatment in these cases is retention and large size. The pathogenesis in the jejunum is found in the abnormal behaviour of muscle fibres in contraction and relaxation, and the jejunal diverticula are not responsible for symptoms. The secondary or traction diverticula occur chiefly in association with an adherent gall bladder and are not of very great significance. It is found that the walls of these diverticula contain muscle fibres.

W. L. GRAHAM

#### The Hereditary and Familial Factor in Hypochromic Anæmia with Achlorhydria.

Barrow, W. H., *Ann. Int. Med.*, 1934, 7: 1135.

Achlorhydria associated with hyperchromic anæmia, as in pernicious anæmia, has long been recognized. Barrow reports its association in several members of a family with an anæmia in which the colour-index was less than I. The family was comprised of three sisters, and the six daughters of one of them. The three sisters had always been anæmic according to the information given by the patient, but the existence of achlorhydria was not known in these cases. The six daughters of one of these women were anæmic, but only three were available for gastric analyses. These three however, showed diminution in the gastric acidity. Two had complete achlorhydria; the other had hypochlorhydria.

MADGE THURLOW MACKLIN

#### Therapeutics

##### The Treatment of Circulatory Failure.

Warfield, L. M., *Ann. Int. Med.*, 1934, 7: 981.

Cases of circulatory failure may be classified into two groups, (1) those accompanied by increased blood volume, and (2) those accompanied by decreased blood volume. Wollheim calls the first plus, and the second minus decompensation. The majority of the former are chronic and cardiac in origin, while the majority of the latter are acute and peripheral in origin.

The acute cases of minus decompensation correspond to circulatory failure in all the severe infections including pneumonia, the bronchopneumonia of grippe, and the toxic infectious diseases. In this type of circulatory failure, the following four conditions are found: (1) decreased blood volume and insufficient return flow; (2) concentration of the blood; (3) decreased blood chlorides; and (4) low venous pressure. With the lowered venous pressure the diastolic filling of the heart is lessened, the heart speeds up, and, as the pulse becomes smaller, the blood pressure falls until a point is reached when there is not diastolic pressure sufficient to carry on the circulation in the coronary arteries. The decreased blood volume is the result of increased osmotic pressure in the tissues due to katabolic changes initiated by the toxæmia.

Treatment should be directed toward correcting the four conditions listed above. In certain cases, the head-down position and crowding fluids by the mouth will suffice. In general, saline solution and 10 per cent glucose should be given intravenously in amounts up to 3 to 4 litres, or over, daily. Also, one can use transfusions of blood, or 6 per cent acacia solution, about 500 c.c. every 3 or 4 days. Blood not only increases and maintains blood volume and introduces important ions such as Ca, Na, and K, but adds oxygen-carrying red cells, which is important in the presence of anæmia.

Drugs to be recommended are those which increase blood volume. These are strychnine in adequate doses, caffeine sodium benzoate, metrazol, adrenaline and pitressin. Adrenaline may be added to the saline-glucose transfusion. Digitalis, except when auricular fibrillation exists, is contraindicated, chiefly because it decreases blood volume.

H. GODFREY BIRD

##### Rational Treatment of the Anæmia Patient.

Murphy, W. P., *Ann. Int. Med.*, 1934, 7: 939.

Rational treatment is possible only after a correct diagnosis has been made. This may be possible in some instances only during the time that the anæmia is present. The prompt and striking increase in reticulocytes during the ten days immediately following the intra-

muscular injection of liver extract is practically limited to patients with pernicious anaemia in relapse, and this therapeutic test may be of aid in making the diagnosis.

The author cites observations which suggest that in pernicious anaemia the potent substance, when injected in excess of immediate needs, is stored for later utilization. Following the initial intramuscular injection of extract from 400 grams of liver, and without subsequent injection, the red cells have been found to increase in some instances at rates as high as 135,000 cells a day for 28 days. Although a number of patients have remained in excellent health with the injection of extract from 100 grams of liver at intervals greater than four weeks, it would seem wiser to give the injections at intervals of four weeks or less. Iron in large doses is often of value in pernicious anaemia, especially for those patients taking liver extract.

Studies carried out in the author's laboratory have shown that large amounts of whole liver may be substituted for iron in the treatment of patients with idiopathic hypochromic anaemia. The liver, however, is not superior to the iron, and is more difficult to take. When liver is given together with iron, the effect is greater than with either iron or liver alone. Liver extract, given intramuscularly, has no apparent effect on the formation of haemoglobin if given alone, but if given with large doses of iron by the mouth there results a more rapid response of the haemoglobin and of the red cells than occurs with the use of a similar amount of iron alone. The preparations containing iron and copper have produced no effects greater than might be expected from the iron contained therein. Ferrous carbonate, 60 grains daily, and ferric ammonium citrate, 45 grains daily, have produced satisfactory clinical results. Evidence available indicates that larger doses of iron are not more effective, and are, therefore, generally unnecessary.

H. GODFREY BIRD

**The Ketogenic Diet in the Treatment of Infections of the Urinary Tract.** Robb, D. C., *Brit. M. J.*, 1933, 2: 1158.

Sixteen cases of urinary tract infection, treated by ketogenic diet, are presented. The details of dietary treatment are given. The ketogenic diet had the effect of increasing the hydrogen-ion concentration of the urine in all but one case; there was a rapid initial fall in pH, a maintained low level till the end of the third week, and then a tendency for the pH to become irregular and rise slightly. Acetonuria was always present, but varied greatly in amount from case to case; not corresponding with the degree of urinary acidity present. Five patients were cured completely, the urine being sterile on repeated culture; in these cases a pH of about 5.4 was reached and maintained.

Four were successful only after the addition of ammonium nitrate to the treatment, and two others, after hexamine. Five patients were improved, but not cured. In each case the ketogenic diet was instituted by stages, and the ketogenic-antiketogenic ratio was determined in each case by simple calculation. An average 3:1 ratio diet would be P. 64 grm., C. 19 grm., and F. 249 grm. Little gastric upset was produced by the diet, and all the patients left hospital in excellent health. It was felt that this method of treatment was unsuitable for use in out-patient clinics.

W. FORD CONNELL

### Hygiene and Public Health

**Silicosis among Granite Quarriers.** Bloomfield, J. J. and Dreessen, W. C., *Pub. Health Rep.*, 1934, 49: 679.

It is a common belief that granite quarrying is not so dangerous as granite cutting in enclosed sheds. The authors report a study of a typical quarry in Vermont. Dust counts were made of air samples and 39 drillers who presented themselves voluntarily were examined by clinical and radiographic methods. Dust counts in millions of particles per cubic foot of air varied from an average of 144.4 to 36.9, for drillers. Other workers were exposed to an average of 5.8. When it is remembered that counts over 10 million are considered dangerous to granite workers it is apparent that a real hazard exists in this work. The examination of the 39 drillers showed that 10 were suffering from silicosis. Two out of 4 workers with ten or more years of exposure, and 4 out of 5 workers, with twenty or more years of exposure, were suffering from silicosis. It is suggested that the only solution of this problem lies in the removal of the dust at its source. Wet drilling is recommended where possible, and also the use of the Kelley dust trap.

FRANK G. PEDLEY

### Urology

**Aseptic Ureter-intestinal Anastomosis.** Higgins, C. C., *J. Urol.*, 1934, 31: 791.

The procedure described is similar to the transfixion suture method of Coffey, in that a fistula is established between ureter and bowel without actually opening the bowel at operation. In the Coffey method, however, the ureter is severed at the point of transplantation, and obstruction is present for 48 to 72 hours until the fistula is established. With the author's method the normal flow of urine is not interfered with and bilateral simultaneous implantation is possible. The abdomen is opened and posterior parietal peritoneum incised over the ureter, which is then freed for 8 cm. The site of implantation in the recto-sigmoid is then selected, and an incision of 6.5 cm. is made

along one of the longitudinal bands down to the mucous membrane. Lateral separation of serous and muscular layers provides a trough for the transplanted ureter. The ureter is then brought into position, and 1 cm. from the lower edge of the incision in the bowel a silk suture is passed through the wall of the ureter into the lumen, then through the mucous membrane of the bowel, picking up the gauze which has been wrapped about a rectal tube and placed in the rectum previously to operation; it is then tied tightly. The muscular and serous layers are now reapproximated and the post-parietal peritoneum closed. The fistula forms in 36 to 60 hours, and during this time there is no interference with the normal continuity of the ureters. There appears to be very little clinical reaction after the operation. It has been performed on dogs in eight cases with excellent results. After the fistulae are established the bladder is removed and ureters ligated below the anastomosis. In dogs this has been done intraperitoneally, and in human cases, extraperitoneally.

N. E. BERRY

#### Cystectomy for Cancer of the Bladder in the Male.

Coffey, R. C., *Trans. West. Br. Am. Urol. Ass.*, 1933, 2: 94.

The early diagnosis of bladder tumours is possible because it is an irritable organ where any disturbance asserts itself early, and also because of exact diagnostic methods. Despite this, and despite the late appearance of metastases, a great majority of the cases treated by fulguration and radium tend to return with ultimate bad results. Since the introduction of satisfactory methods of transplanting the ureters into the large intestine cystectomy has become a feasible procedure, and will, if performed early, bring a cure in a larger percentage of cases than follows operations for cancer affecting any other organ. The author suggests therefore that one should not wait too long before dealing with these growths before undertaking radical procedures. In men, cystectomy and transplantation of the ureters should be carried out at one sitting, as it is simple when the abdomen is already widely open, and the better drainage afforded by the gauze pack in the vesical space more than compensates for the additional operation of cystectomy. The bladder is removed in retrograde fashion, starting at the neck, severing the urethra, and pulling the prostate upward and forward. The ureteral transplantation is performed by Technique 2, in which large catheters are anchored in the ureters during convalescence. An analysis is presented of 11 cases treated in this way with very satisfactory results. Excellent illustrations of bladders removed with growths are included.

N. E. BERRY

#### Ophthalmology

**The Influence of Ametropia on Certain Infections of the Adnexa of the Eye (lids, lachrymal tract).** Robert, G., *Ann. d'Ocul.*, 1933, 170: 663.

Fatigue of the eyes, though slight, when prolonged, even when caused by ametropia of small degree, affects in certain cases the lids and lachrymal tract and the eye itself. In these cases there are present asthenopia, varying according to the age of the patient, and also infectious processes, particularly if the surrounding cavities are infected which make the patient susceptible.

In the presence of infectious manifestations, it is necessary to make a thorough examination of the refraction and to correct this as nearly as possible. Small degrees of ametropia should not be neglected. Except in rare cases a normal eye as a whole is not easily accessible to infection, so that if this does appear, and particularly if it becomes chronic, it is necessary to look for a local cause. We begin by correcting the ametropia and follow this by the usual orthodox treatment.

These ideas are the same as those expressed by Prof. Lagrange on the necessity of complete refractive correction as the basis of all satisfactory treatment of these eye conditions.

S. HANFORD MCKEE

**The Value of the Mantoux Reaction as a means of recognizing the Tuberculous Character of Ocular Affections.** Braun, R., *Ann. d'Ocul.*, 1933, 170: 267.

Brown experimented with the Mantoux (Mendel) reaction in 200 cases, and concludes that it is not at all an aid in the diagnosis of tuberculosis. Comparing cases with tuberculosis and without tuberculosis, the reaction was found positive in only 20 per cent more of the first group than in the second. He does not believe that the Mantoux reaction assists in any manner in the diagnosis of ocular tuberculosis.

S. HANFORD MCKEE

**Ocular Complications of Acne Rosacea.** Adamantiadis, B., *Ann. d'Ocul.*, 1933, 170: 760.

The effect of acne rosacea of the face, on the eye, particularly on the cornea, was first described by Arlt in 1864. Since that time there have been many communications by different authors, with the complete study by Peters and his pupils Erdmann and Triebenstein, who determined the different forms in which this malady shows itself in the eye.

Among 5,000 patients Adamantiadis saw 3 cases of ocular rosacea, and from reference to the ordinary text-books the writer concludes that the condition is a rare one. One of the principal features of rosacea is the telangi-

tases of the already congested coats. They are found usually in the locality of the rosacea, on the conjunctiva and the sclera and part of the cornea. The lesion is a localized telangiectasis, of an eruptive nature. The veins appear dilated and tortuous around the acne lesion. Another feature of the malady, equally important, is the chronicity of the manifestations, discouraging alike both for the patient and the physician.

Of the 3 cases reported, the first two are not of special interest. In the third case, however, the patient, of 7 years, had had the lesion since his first year. The lesions of the anterior parts of the eye had healed and recurred constantly, taking a chronic course very slightly different from that usually seen.

S. HANFORD MCKEE

#### Neurology and Psychiatry

**Spinal Cord Tumours.** Grant, F. C., *Am. J. Surg.*, 1934, 23: 89.

This is a study based upon a series of 18 verified spinal cord tumours. A relatively high proportion of the benign fibroblastic type of tumour was found, in comparison with the brain where the infiltrating gliomas are the more common. Pain, which was increased by coughing or straining, was the first symptom of cord tumour in 13 cases. Fourteen patients had numbness or tingling in areas below the level of the tumour and in all of these cases subjective sensory disturbances preceded motor disturbances. Pressure on the cord is seldom limited to one side only. Hence the Brown-Séquard syndrome is rarely clean-cut, and frequently a reversal of sensation occurs, with the greatest sensory loss upon the same side as the tumour and more motor disturbance on the opposite side. In the development of motor symptoms one lower limb usually becomes involved before the other. In 17 of the 18 cases hyperactive reflexes with clonus and Babinski's sign were recorded on one or both sides.

The most important single factor in securing a favourable result is early diagnosis and removal of the tumour. The type of tumour and its position in relation to the circumference of the cord cannot be determined with certainty prior to operation. In the early stages when atypical histories and bizarre neurological findings make diagnosis more difficult recourse must be made to certain mechanical methods of localization. Every case of suspected cord lesion should have a lumbar puncture, plus a Queckenstedt test and estimation of the spinal fluid protein. If the sensory level is definite, and if a simple Queckenstedt test reveals no block, and the protein of the fluid is normal, the condition is probably not tumour. If further verification is needed a combined cisternal and lumbar puncture, with a Quecken-

stedt test and comparison of the protein content of the fluid from these two situations, should be made. If there is any indication of block, and if the sensory level is uncertain, then opaque oil should be employed.

FRANK A. TURNBULL

**Multiple Sclerosis and Amyotrophies.** Davison, C., Goodhart, S. P. and Lander, J., *Arch. Neurol. & Psychiat.*, 1934, 31: 2.

Finding that 12 out of 20 cases of multiple sclerosis coming to autopsy and 17 of 110 cases studied clinically showed atrophy of one or more groups of muscles, the writers feel that such a high incidence of correlation merits further study. The appearance of muscular atrophy would tend to even further confuse the protein clinical picture of multiple sclerosis with that of amyotrophic lateral sclerosis.

The autopsy findings on three cases are presented. The muscular atrophy was due to destruction of the anterior horn cells by the invasion of a disseminated plaque. This was most frequent in the lower cervical region and hence the intrinsic hand muscles were the commonest group involved. Of the twelve cases in this atypical group four showed well marked mental changes.

G. N. PATERSON-SMYTH

**Pellagra in Association with Chronic Alcoholism.** Zimmerman, H. M., Cohen, L. H. and Geldea, E. F., *Arch. Neurol. & Psychiat.*, 1934, 31: 36.

The authors describe three cases of chronic alcoholism associated with findings in the nervous system suggestive of pellagra. One case presented the typical cutaneous lesions, and all three showed very marked improvement on a high-vitamin diet. Official examination of the nervous system showed, apart from mental changes of a deteriorative type, evidence of a pyramidal lesion (increased deep reflexes, absent abdominal and positive Babinski and Hoffman signs), and sensory loss. There was also degeneration to a lesser extent in the peripheral nerves. The pathological findings showed a fairly characteristic neuronal change of the so-called axonal type, associated lipoid deposits, and hyalinization of the capillaries. Much more striking however was the severe grade of demyelinization found in the posterior and lateral columns (pyramidal tracts). Their conclusion is that chronic alcoholism, by producing a loss of appetite or by interference with assimilation, led to a vitamin deficiency producing the pellagrous condition.

G. N. PATERSON-SMYTH

### Dermatology

**Malignant Melanomas Arising in Moles: Report of Fifty Cases.** Butterworth, T. and Klauder, J. V., *J. Am. M. Ass.*, 1934, 102: 739.

Malignant change may occur in a mole at any age, but the average age is 47. It is much more common in males and occurs almost exclusively in the white race. In an analysis of 598 cases, malignant melanomas developed from moles located as follows: head, 16.5 per cent; neck, 7.7 per cent; trunk, 15.5 per cent; genital and anal regions, 2.7 per cent, and foot, 52.3 per cent. Contrary to popular belief, malignancy is just as likely to develop in brownish coloured melanomas (moles) as in the deeply pigmented ones. Trauma appears to play a rôle in the onset of malignancy in about 20 per cent of cases. The first evidence of malignant change is increase in size, and this may be followed by, or associated with, increase in pigmentation and bleeding. Melanuria and generalized pigmentation occasionally occur.

When malignancy is suspected, the authors advocate wide excision of the affected site, preferably by electro-surgery. This is followed at once by heavily filtered, high voltage x-ray to the operative site and to the neighbouring lymph glands. If the malignant lesion is on an extremity, amputation should be seriously considered. In the 50 cases reported, 26 patients were dead in two years and a half, 6 are still living after three years, and 14 are still living, but the duration of time since the onset of the malignancy is less than three years.

In conclusion, the authors offer some very sage advice regarding the treatment of melanomas (so-called moles or nævi). "Thorough destruction, including healthy tissue surrounding the lesion and beneath it by means of the electro-cautery, electro-dessication, or surgical excision affords the safest means of removing pigmented nævi. The nævus should be entirely destroyed at one operation. To treat the lesions by painting with acids, by applying carbon dioxide snow, by electrolysis, strangulation by tying a string around a pedunculated lesion, or any treatment given at short intervals are dangerous procedures which constitute irritation and afford opportunity for malignant change. In propaganda for the control of cancer, this principle cannot too strongly be emphasized."

NORMAN M. WRONG

**Lymphogranuloma Inguinale, the Fourth Venereal Disease: Its Relation to Stricture of the Rectum.** Cole, H. N., *J. Am. M. Ass.*, 1933, 101: 1069.

This disease has been more or less recognized for seventy-five years, but Nicolas, Favre and Durand, in 1913, were the first to give good clinical and histological descriptions of it. Numerous cases have been reported from France, South America, Cuba and lately from

the United States. Cole's clinic in Cleveland has furnished the first complete reports and the greatest number of cases. Frei, in 1925, reported an intracutaneous test which has proved to be specific in this disease and of great value in the diagnosis of the obscure cases.

An excellent review of the clinical course is given by the author. This consists of an evanescent primary sore and then lymphatic enlargement, softening, and the formation of multiple fistulæ. The non-syphilitic, non-tuberculous, chronic inflammatory reaction about the rectum and anus is next discussed. The type which has multiple fistulæ and progresses to marked scar formation and anal stricture is often due to lymphogranuloma inguinale. In these cases, the Frei test is positive. This anorectal syndrome is much more common in the female than the male.

NORMAN M. WRONG

### Anæsthesia

**Spinal Anæsthesia in Hypertension.** Hyman, A. S., *J. Am. M. Ass.*, 1933, 101: 1410.

The depressor action of spinal anæsthesia has long been known. In 1931 a study of 3,000 administrations was made. Some drop in both systolic and diastolic levels of the blood pressure occurred in 92.4 per cent. The fall averaged from 10 to 38 mm. of mercury in patients exhibiting no cardiovascular disease. In those with high blood pressure the depressor effect was most marked, the higher the systolic level, the greater being the fall. In one case it was from 260 to 110, and in another from 248 to 128. In practically all cases with a pre-operative systolic level of 220 and above there was a drop of 50 mm. This was suggestive for the treatment of arterial hypertension, approaching the prodromal phase of cerebral haemorrhage. Venesection is often life-saving, but the secondary anaemia frequently associated with this condition may be markedly accentuated by the removal of large quantities of blood. Besides the actual fall obtained by the removal of 500 to 1000 c.c. is not more than 30 to 50 mm. The first patient treated by spinal anaesthesia was a man, aged 58, with signs and symptoms of impending cerebral haemorrhage. His blood pressure on admission was 244/120. He was given  $\frac{3}{8}$  of the usual dose of tropocaine, and within 20 minutes the blood pressure fell to 180/110. Ten minutes later it was 168/105. There were no unfavourable cardiac signs, and within an hour nearly all the previous symptoms, with the exception of the posterior headache, had cleared up. Blood pressure readings were taken every 4 hours for the next week and showed a slow rise in the systolic component to 210 mm. The patient remained free from symptoms for several months. This case was followed by 11 others of the same type with the same general response.

ARTHUR WILKINSON

## Obituaries

**Dr. Thomas P. Bradley**, of Sarnia, Ont., died on June 30, 1934. He was born in 1873 and graduated from Trinity University in 1898. He is survived by his widow, formerly Helen G. McPherson.

**Dr. Antoine Paul Cartier** of St. Hyacinthe, Que., formerly Conservative member of the Quebec Legislative Assembly for the county of St. Hyacinthe, died on July 10, 1934, at the advanced age of 85 years. He was born at St. Antoine-on-the-Richelieu on June 17, 1849, the son of Narcisse Cartier. He was related to Sir George Etienne Cartier, one of the fathers of confederation. He conducted his classical studies at the Seminary of St. Hyacinthe and studied medicine at Montreal, receiving his degree in 1873 from Victoria University, Cobourg. After practising his profession at Coaticook for about two years he established himself at St. Madeleine, where he practised 44 years.

Dr. Cartier was a pioneer in the parish of St. Madeleine, mayor for several years, prefect of the county, and governor of the College of Physicians and Surgeons. He held an honorary doctorate from Bishop's College, Lennoxville (1895). He had the distinction of being the only Conservative member which the county of St. Hyacinthe has ever sent to the provincial legislature.

Dr. Cartier is survived by his wife, née Marie Ernestine Lenoble-Duplessis; and three sons, Jacques Narcisse, of St-Gabriel de Brandon, Jean, of Montreal, and Paul, professor of chemistry at the University of Montreal; two daughters, Pauline, wife of Dr. J. E. A. Collette, and Alice, wife of W. Déziel, Montreal.

**Dr. Robert Crosby**, one of the most prominent and highly respected members of the profession in Vancouver, died suddenly on July 5th from coronary thrombosis.

Dr. Crosby was born at Campbellford, Ont., in 1870. He graduated from Toronto University in 1899. After practising for four years at Byng Inlet he went to New York to pursue post-graduate studies, finally becoming house surgeon at the Brooklyn Eye and Ear Hospital. In 1908 he settled in Vancouver, practising ophthalmology and otology, and soon became widely known throughout British Columbia. He was connected with the Vancouver General Hospital from 1915, his being one of the first appointments when the Out-Door Department was opened. Later, he was appointed to the senior staff, and in 1931 to the consulting staff. In 1901 Dr. Crosby married Miss Isabelle Peters, a sister of the late Dr. George A. Peters, of Toronto. He is survived by his widow, two sons, and two daughters. A firm adherent of his faith, he was for many years an elder of St. John's United Church.

Dr. Crosby was one of those physicians who add lustre to the profession through the respect of the community, earned by that conscientious and skilful treatment of all classes of patients which was exemplified in his work as ophthalmic surgeon to the Indian Department. Of a rather retiring disposition, he was, nevertheless, a man of marked force of character; he never hesitated to state his position on a question, but with a characteristic frank straightforwardness which left no rancour behind it. Like Chaucer's Knight, he was "honoured for his worthynesse".

COLIN GRAHAM

**Dr. J. Emile Daignault**, of Sherbrooke, Que., died suddenly on July 11, 1934, at the Saint Vincent de Paul hospital. He was born in 1886 at Lawrenceville, the son of Dr. and Mrs. Alphonse Daignault. He conducted his classical studies at the Seminary of Ste. Marie de Monnoir, and his medical studies at the

University of Montreal, from which he graduated in 1912. He is survived by his widow, née Blanche Paradis; two children; a sister and a brother.

**Dr. Louis Doray** died during the first week of July, 1934, in Montreal, at the age of 60 years. He had practised medicine for more than thirty years at Pointe-du-Lac near Three Rivers. He is survived by three brothers, Arthur and Henry, Dr. Raymond Doray, all of Montreal; and one sister, Cécile.

**Dr. Aubrey Taylor Fuller**, of Vancouver, died at his home, on July 15, 1934. The late Dr. Fuller was born at Truro, N.S., in 1875. He received his B.A. at Mount Allison in 1897, and his M.D., C.M., at McGill in 1901. He had practised in Vancouver for thirty-one years, a quiet hard-working general practitioner of the old school. Never active in association affairs, he was nevertheless known to his intimates as a man of rare judgment, kindly and conscientious, and with a keen and sparkling wit. He had studied in London and Dublin, and his reminiscences were at all times interesting. He served throughout the war with the C.A.M.C.

**Dr. Thomas Symes Genge**, of Verona, Ont., who practised medicine at Parham and Verona for thirty years, died recently at Verona. He was born in 1870 and was a graduate of Queen's University, securing his degree in 1901. His widow, three sisters, and three brothers survive.

**Dr. Georges Geron**, of Sainte-Geneviève de Pierrefonds, died on July 1, 1934, aged 80 years. He was a graduate of the medical school of the University of Bishop's College, Montreal, in 1879.

**Dr. Gerald Stinson Glassco**, of Hamilton, Ont., member of the local Lunacy Commission and Director of the Mental Hygiene Clinic of the Board of Health, died on July 22, 1934, in his 63rd year. He was born in Hamilton and had lived there all his life. He attended Central School, Central Collegiate Institute, and graduated from the University of Toronto in 1893. Later, he took a post-graduate course at St. Bartholomew's Hospital, London, and had practised in Hamilton since his return. The late Dr. Glassco was a pioneer in psycho-analysis in Canada, commencing this phase of medical work in 1915.

He became recognized quickly as an able specialist and consultant and as a member of the local Lunacy Commission and director of the Mental Hygiene branch of the Health Department performed outstanding service.

In religion he was an Anglican and a member of Christ Church Cathedral. Surviving are his widow; three sons, Ivan, of Hamilton; Allan Ewart, London, Eng., member of the Royal Tank Corps; Colin Stinson, of Montreal; and a daughter, Margaret, at home.

**Dr. Henry Howitt, Sr.**, of Guelph, Ont., passed away suddenly at his home on July 22, 1934, in his eighty-sixth year.

Dr. Howitt was internationally known for the work which he did in the development of special techniques for perforation of the stomach and spinal surgery, and he had gained a wide reputation throughout Canada and the United States. He was one of the first pupils of Lawson Tait, the famous English surgeon. He was in practice in Guelph for over forty years.

A lifelong resident of the district of Guelph, Dr. Howitt was born at the Howitt homestead, the Grange, Guelph Township, a son of the late John Howitt and

Margaret McIntosh. He studied at Victoria and Trinity Universities, graduating as gold medallist at the latter in 1873. He became a member of the Royal College of Surgeons the following year, and in 1875 commenced to practise in Guelph, continuing until 1918.

Dr. Howitt became a Fellow of the American Association of Obstetricians and Gynaecologists, and he was a foundation member of the American College of Surgeons. He was also a former President of the Guelph Medical Society and St. George's Society. Dr. Howitt was also elected an honorary member of the Western Medical Association for meritorious work. He was a former President of the Guelph and Ontario Investment and Savings Society, senior surgeon of the Guelph General Hospital and St. Joseph's Hospital.

In 1875, Dr. Howitt married Grace Davidson, and on her death married Clara Kate Skinner, of Braeside, Guelph. He is survived by his widow, and four children of his first marriage: Mrs. P. D. Ivey, Oakville; J. R. Howitt, K.C., and Dr. H. O. Howitt, Guelph, and Mrs. E. P. Flintoft, Montreal.

**Dr. Louis Legault**, of Cornwall, Ont., who had been in practice in Cornwall for the past year, died suddenly at his home in East Cornwall on July 11, 1934. Retiring the previous night in his usual health, Dr. Legault failed to arrive at his office in the morning. Later he was found dead in bed.

Dr. Legault was born at St. Isidore, Ont., 59 years ago and he was a graduate of University of Montreal (1901). He practised at St. Stanislas de Koska, Que., and later at Chrysler, Ont. Subsequently he opened an office in Cornwall. He leaves three sons and a daughter. His wife died two years ago.

**Dr. Victor J. Levasseur**, of St. Johns, Que., died in the St. John's Hospital after a week's illness. He was born in St. Angèle de Laval in 1886, studied at the University of Montreal, and since 1912 had practised in St. Johns.

He leaves one son, James; his wife had predeceased him.

**Dr. Thomas McCurdy**, of Coaticook, Que., died about August 5, 1934.

The late Doctor McCurdy was a native of Orms town, Que., and was in his sixty-seventh year. He studied at Huntington Academy and took his degree in medicine at McGill University in 1889. He first practised his profession in Sutton, then in Sawyerville, and for the past twenty-nine years in Coaticook. In 1893 he married Miss Olo Knight, of Coaticook, who survives him with one daughter, Eloise.

Dr. McCurdy was district physician for the Canadian National Railway. He was a great sportsman and was actively interested in the local Chamber of Commerce, in which he occupied several positions of trust.

**Dr. Fulton Schuyler Vrooman**, of London, Ont., formerly superintendent of the Ontario Hospital on Queen Street, Toronto, and of the provincial mental institution in Mimico, and who for the last four years had held a similar post at the Ontario Hospital in London, died on July 10, 1934, in Victoria Hospital, London. He had undergone an operation for appendicitis.

Dr. Vrooman was born in Lindsay, Ont., in 1882 and was a graduate of the University of Toronto (1904). He served overseas with the C.A.M.C. and was stationed at Orpington, Kent. He also, later, was in charge of the first hospital for shell-shocked men, located in Cobourg, Ont.

## News Items

### Great Britain

**The British Industries House.**—Another important stage in the development of British Industries House, London, which is to provide a permanent and comprehensive marketing centre for the Empire, and which was opened on July 2nd, was reached on July 19th when Lord Derby opened the Medical Section and Model Hospital suite.

The hospital unit, which is claimed to be the most up-to-date in the world, has two completely equipped operating theatres for major and minor operations, a clinical laboratory and rooms for surgeons, anaesthetists and sisters. There is also a sun balcony for convalescent patients. Apart from the hospital there are two other medical sections. In one is displayed a full range of British-made instruments and apparatus, to meet every need of the medical and surgical side of hospital work. The other section is a manufacturers' pattern and sample department for commodities needed on the lay side of hospital maintenance.

The object of the twelve-bed ward and the two medical sections is to provide the overseas purchaser with one central organization in which he can find all the goods in which he may be interested, and thus be saved the time and expense of travelling to different parts of the country.

The Reception Committee at the opening of the Medical Section was Lord Dawson of Penn, President of the Royal College of Physicians; Lord Horder, Physician in Ordinary to the Prince of Wales; Lord Moynihan, Chairman of the Army Medical Advisory Board; Sir Humphry Rolleston, Bart., Physician Extraordinary to the King; and, Sir Holburt J. Waring, President of the Royal College of Surgeons. In administering the Medical Section, British Industries House has the advantage of the services of the following Advisory Council: Mr. Alfred Cox, O.B.E., M.A., M.B., LL.D., (Chairman); Mr. A. R. Melhuish, M.P.S.; Sir Crisp English, K.C.M.G., F.R.C.S.; Mr. E. P. Poulton, M.D., F.R.C.P.

A qualified medical practitioner and technical experts are attached to the section in order to assist intending buyers.

Apart from the individual exhibitors representing numerous industries who have already installed their showrooms in British Industries House, plans are nearing completion for geographical and industrial group exhibits. Prominent among these is Sheffield stainless steel for which a large area has been reserved. Various townships are also negotiating for space in which to display their products.

One of the most interesting features of British Industries House is the luxuriously appointed Buyers and Merchants Club, which enables business to be transacted in pleasing surroundings.

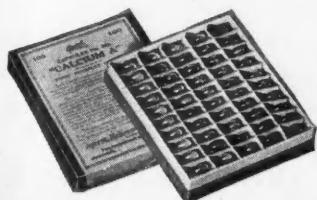
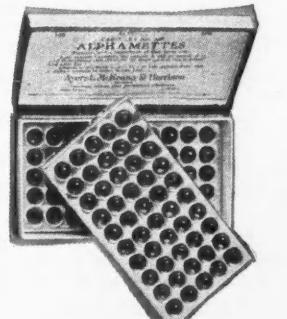
British Industries House is one of the largest and most completely equipped of London's modern buildings. It occupies a prominent central position adjoining Marble Arch and is under the control of five insurance companies.

### British Columbia

At the time of writing this the medical profession and the community as a whole are profoundly shocked over the very serious injuries sustained by Dr. A. P. Procter, on August 3rd. Entering his office at lunch time, he was shot down without warning by a man seated in the waiting room. Latest reports indicate that he has a haemothorax, but that he is holding his own, which under the circumstances must be regarded as encouraging.

During the past month, medical men throughout the Province have received questionnaires relating to Health Insurance, one from the Council of the College,

# *this question of* **HALIBUT OR COD**



Unquestionably, Halibut Liver Oil has definite therapeutic merit—so has, of course, Cod Liver Oil. But Halibut Liver Oil cannot take the place of Cod Liver Oil. Halibut Liver Oil is being widely advertised as a substitute for Cod Liver Oil. It is NOT a true substitute and cannot properly be described as "Cod Liver Oil by the drop." Halibut Liver Oil is rich in vitamin A and provides an excellent medium for VITAMIN A THERAPY, but, being relatively low in vitamin D, it cannot be used economically as an anti-rachitic agent.

Cod Liver Oil is the "gold standard" of vitamin A and D therapy, and long clinical experience has established the fact that the vitamin A and D ratio in Cod Liver Oil is sound and practical. Every physician appreciates the value of Cod Liver Oil "by the teaspoonful," and it is probable that Halibut Liver Oil has had its greatest appeal because of the convenience of its capsule form. Where convenience is a factor in Cod Liver Oil therapy we offer Alphamette Liquid, and the capsule forms, Alphamettes and "Calcium A." These three products are prepared for the convenient application of Cod Liver Oil therapy and faithfully retain the same "gold standard" values of vitamins A and D as exhibited in good medicinal Cod Liver Oil. Each Alphamette exhibits the full vitamin value of three teaspoonsfuls of Cod Liver Oil and each "Calcium A" Capsule that of one teaspoonful in association with organically combined calcium and phosphorus. The choice as between Halibut Liver Oil and Cod Liver Oil rests primarily with the physician. We endeavour to supply products which meet the demands of the profession, and therefore, offer capsules of Halibut Liver Oil "Plain" and "250-D" which conform with the standards of potency set up by the Council on Pharmacy and Chemistry of the A.M.A.



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the other from the Government. It seems certain that legislation will be introduced at the next session of the House.

Dr. Vernon E. Ardagh, a veteran medical missionary of the north, has recently retired, and now resides in Vancouver. Space does not permit more than a brief outline of his very interesting career. A graduate of Edinburgh in 1885, he had been a classmate of Rudyard Kipling at the school made famous to us in "Stalky & Co." His first work was done in British East Africa. In 1889 he came to British Columbia, and conducted a mission at Metlakatla. For years his nearest confrère was at Nanaimo. Since 1901 he has lived at Kitwanga on the Skeena river.

C. H. BASTIN

### Manitoba

The Unemployment Relief Department of the City of Winnipeg has notified the doctors of Winnipeg that the present arrangements for payment for medical services rendered to those on relief will cease on August 22nd. It is expected that another agreement will be reached between the city and the medical profession, but only on the basis of a reduction from the present scale of fees. A suggestion that the city pay a fixed sum per month to be distributed *pro rata* among the doctors did not find favour with the latter.

A complimentary dinner was tendered by his colleagues on August 9th to Dr. J. M. Leney, who is retiring on pension from the post of Medical Director at Winnipeg of the Canadian National Railway. Dr. Leney was presented with a set of matched golf clubs and a leather golf bag.

Sidney Smith, the new President of the University of Manitoba, Mrs. Smith, and their two children were welcomed at Winnipeg on August 7th, on their arrival from Halifax.

Improved operating room facilities at a cost of \$5,000 will be provided at Manitoba Sanatorium, Ninette. Ten thousand dollars will be spent in providing a cottage for a resident physician and improving accommodation for the medical staff.

We are glad to note that Dr. Wm. Boyd, Professor of Pathology in the University of Manitoba, who had received a flattering offer of the Chair of Pathology at Leland Stanford University, California, has elected to stay in Winnipeg.

ROSS MITCHELL

### New Brunswick

On July 17th, Premier L. P. D. Tilley announced that Dr. J. V. Anglin and his associate, Dr. J. Boyle Travers, had both been granted leave of absence for six months, and at the end of the six months, they were to be retired on pension.

Dr. Anglin assumed charge of the Hospital for the Insane in 1904. During his tenure of office, many improvements in methods of treatment and additions to the plant have been made. The institution has grown from a bed capacity of 550 until at present more than 900 patients are under care. For several years, Dr. Anglin was a member of the Council of the American Psychiatrists' Association, and in 1918 he served as President of that body. Dr. J. Boyle Travers has given practically the whole of his professional life to the care of the mentally ill. For 37 years—since 1897—he has been in an executive position in the Provincial Hospital at Lancaster. Both Doctors enjoy the friendship of a wide circle of friends throughout the province, and it is the hope that they will be spared for many years to enjoy a well-earned relaxation from duties which they have carried successfully for such a long period.

At the July meeting of the Commission of the Saint John Tuberculosis Hospital it was announced that there had been established a three months' post-graduate course in tuberculosis nursing at the East Saint John institution.

During the visit of their Excellencies, Lord and Lady Bessborough, to the Province of New Brunswick, they again gave evidence of their interest in hospital affairs by visits to several of the hospitals throughout the Province.

At the recent meeting of the New Brunswick Medical Society, Dr. P. H. Laporte, the retiring president, in his presidential address expressed the hope that state medicine would not soon be found to be a necessity in Canada. Dr. Laporte stressed the usual reasons and arguments against the establishment of state medicine, particularly, that in any form of state medicine the relation between the physician and the patient would necessarily be changed, which he felt would be a change for the worse. Dr. Laporte's address was given considerable space in the local papers, and has brought forth opinions both in favour of his stand and against it. The consensus is that at least in the Province of New Brunswick the necessity for state medicine is not pressing. It is the well-founded belief in this Province, that if the municipalities (failing Federal and Provincial assistance) would make some definite proposal for payment for medical treatment of absolute indigents that the situation would be found satisfactory.

Dr. W. O. McDonald has just returned from a six weeks' post-graduate course in Boston, where he has furthered his studies in the treatment of diabetes.

The Provincial Government, through the Minister of Health, Dr. H. I. Taylor, has announced that biopsy material will be examined free of charge in the case of indigent patients.

A. STANLEY KIRKLAND

### Nova Scotia

Dr. James Angus Doull, a graduate of Dalhousie University, at present Professor of Hygiene and Public Health at the School of Medicine of Western Reserve University, Cleveland, has been elected to an honorary membership in the Royal Sanitary Institute of Great Britain. This membership is limited to thirty, of whom seven are Americans.

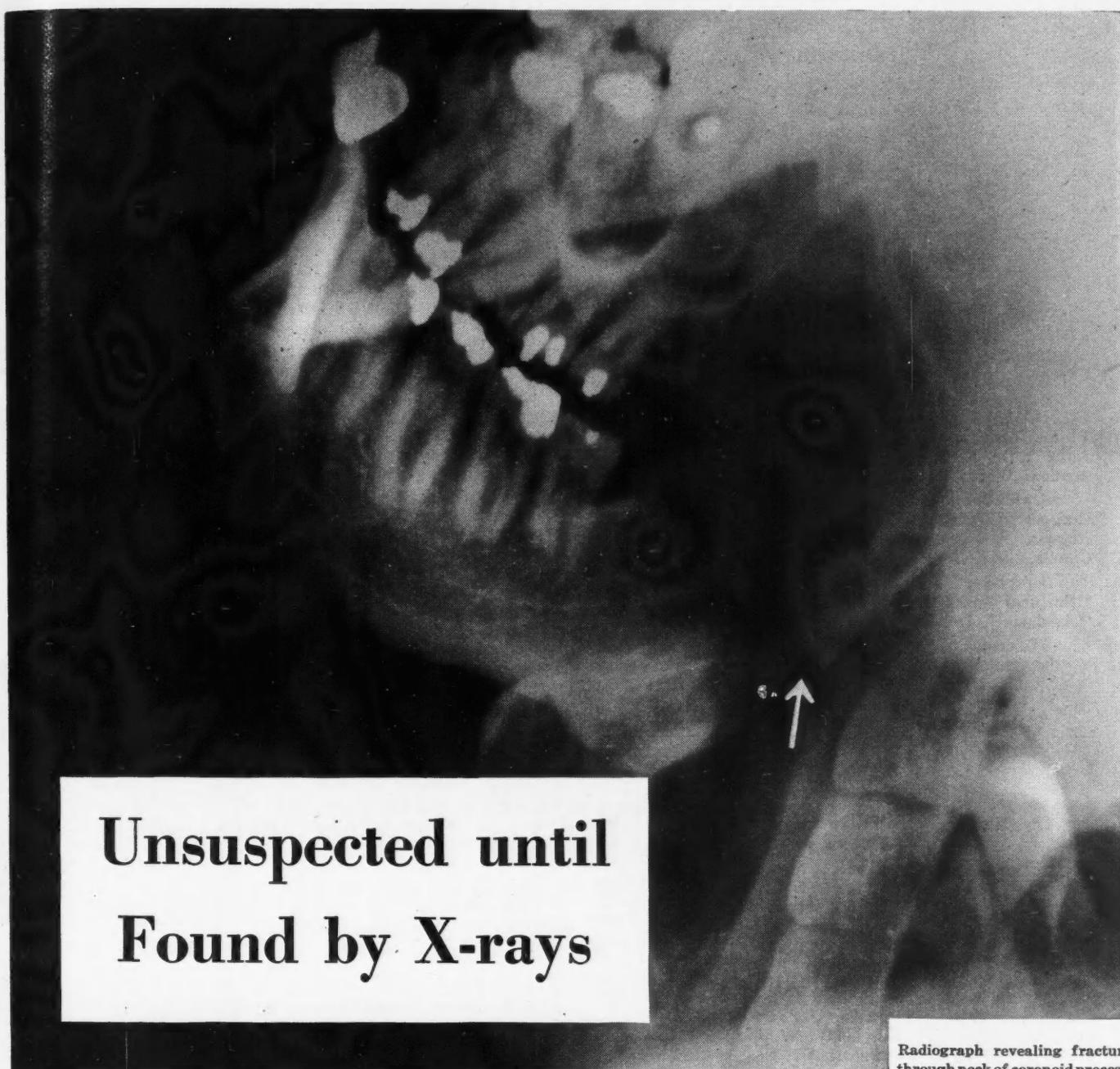
Dr. Yale Brody, a graduate of Dalhousie University, 1934, has left for New York to take up his duties as an intern at St. Peter's Hospital.

Dr. Arthur M. Marshall has returned to Halifax to resume his practice. He spent the past two years working at Edinburgh, where he obtained his Fellowship in the Royal College of Surgeons. He also studied on the Continent where he attended post-graduate courses in medicine.

Dr. John Howard Mueller, Associate Professor of Bacteriology in the Medical School of Harvard University, is spending the summer months working in the Medical Sciences Building of Dalhousie University. Dr. Mueller has gained a world-wide reputation as the discoverer of methionine, an amino-acid which is the product of bacterial metabolism. His present studies are a continuation of his researches into the metabolism of bacteria.

Dr. Montford Haslam, of the Class of 1926, is at present spending a vacation in the province. He is engaged in practice at Concord, New Hampshire, and he is also resident physician in charge of the Health Service of St. Paul's School at Concord.

N. B. DREYER



## Unsuspected until Found by X-rays

Radiograph revealing fracture through neck of coronoid process.

TRAFFIC accidents, industrial accidents, acts of violence bring physicians numerous cases of head injuries. Even though the conditions may be obviously serious, the physical findings may not point to fractures of the jaws. Yet such injury is common in these cases, and early treatment is imperative.

Therefore, a comprehensive radiographic examination should be made as soon as the patient's condition permits. The

possibility of mandibular fractures always should be considered... Several radiographs should be made to determine whether they are present. Since one-third of such fractures are double, both right and left sides should be examined.

Whenever you are called on a case with head injuries, make full use of your radiologist's service. For only radiographs can provide you with the necessary, complete, accurate information.

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## Ontario

The Sixth Post-Graduate Course at St. Michael's Hospital, Toronto, is announced as follows:

*September 10th.*—"Sub-acute combined degeneration of spinal cord", Dr. J. Loudon. "Migraine", Dr. McPhedran. "The nervous patient", Dr. W. Edmonds. *Clinics.*—Staff of Ear, Nose and Throat Department.

*September 11th.*—"Colitis", Dr. A. J. Mackenzie. "Clinical correlation of chest and abdominal conditions", Dr. D. Prendergast. "The peptic ulcer", Dr. J. Daly. *Clinics.*—Staff of the Eye Department.

*September 12th.*—"Clinical correlation of heart and lung conditions", Dr. T. G. Heaton. "The heart in general practice", Dr. A. R. Hagerman. "Clinical diagnosis by laboratory methods", Dr. J. C. Lyons. *Clinics.*—Dr. McPhedran's Unit Medical Wards.

*September 13th.*—"Pneumothorax therapy", Dr. J. Elliott. "Non-tuberculous pulmonary disease", Dr. E. A. Broughton. "A short series of treatment in hay fever", Dr. R. Smylie. *Clinics.*—Dr. Mackenzie's Unit Medical Wards.

*September 14th.*—"Endocrine diseases", Dr. G. Cragg. "Vitamin therapy in practice", Dr. A. Hethington. "Common skin diseases", Dr. F. A. Ireland. *Clinics.*—Dr. Elliott's Unit Medical Wards.

*September 15th.*—"Anæmias", Dr. H. Hall. "Surgical difficulties", Dr. M. H. V. Cameron. "Acidosis", Dr. F. J. Colling.

All doctors are heartily welcome, and no fees will be charged. If further information is desired, please communicate with Dr. W. B. Edmonds, Medical Arts Bldg., Toronto.

## Quebec

The Montreal Medico-Chirurgical Society announce their Second Annual Convention which will take place in Montreal on Friday and Saturday, October 26th and 27th. The program will consist of clinical addresses and special ward demonstrations in all branches of medicine, surgery, and the specialties. These clinical sessions will be conducted by the Fellows of the Society and guests whose names will be announced later. A banquet will be held on the evening of October 26th and on the afternoon of the next day (Saturday) McGill plays the University of Western Ontario at football. The first Convention of this kind, held last year, was conspicuously successful, so much so that it was decided to make it an annual event. All practitioners living in Ontario, Quebec, and the bordering United States are specially invited.

## Saskatchewan

The Honourable H. E. Munroe, Lieutenant-Governor of Saskatchewan, was among the list of distinguished Canadians who received the honorary degree of LL.D. at McGill University convocation in May last.

Dr. Munroe has held the post of Lieutenant-Governor of Saskatchewan since March 31, 1930. He is a native of Glengarry County, Ont. He graduated from McGill in 1903, and has the L.R.C.P. & S., Edinburgh, also his F.A.C.S. He has studied at the Royal Infirmary, Edinburgh, the University College Hospital, and St. Bartholomew's Hospital, London, England.

One of the founders of the city of Saskatoon, Dr. Munroe served overseas, was mentioned three times in despatches and awarded the Order of the British Empire. He was raised to the rank of lieutenant-colonel while serving in the Dardanelles campaign in 1916.

LILLIAN A. CHASE

## United States

**The Seventh Annual Graduate Fortnight of the New York Academy of Medicine.**—The Seventh Annual Graduate Fortnight of the New York Academy of Medicine will be devoted to a consideration of gastrointestinal diseases. The Fortnight will be held October 22nd to November 2nd.

Sixteen important hospitals of the city will present coordinated afternoon clinics and clinical demonstrations. At the evening meetings prominent clinicians from various parts of the country who are recognised authorities in their special lines of work will discuss the various aspects of the general subject.

A comprehensive exhibit of anatomical, bacteriological and pathological specimens and research material will be shown. Many of the exhibits will be demonstrated.

Among the subjects to be presented at the evening meetings and in the hospital programs will be: general principles involved in the diagnosis of gastrointestinal diseases—medical, surgical, roentgenological; constipation; diarrhoea; physiology of the gastrointestinal tract; diseases of the pancreas, especially acute pancreatitis and its treatment; diseases of the oesophagus; functional diseases of the stomach; disorders of the gastrointestinal tract in children—*infections, management, surgery in infants and children; diet in relation to gastrointestinal diseases in infancy; clinical examination of the patient from the surgeons' and the internists' points of view; demonstrations of diets used in treatment; peptic ulcer—medical discussion—surgical discussion; carcinoma of the stomach; chronic lesions in the paracæcal region; acute appendicitis; peritonitis; gall-bladder and biliary passages—medical discussion—surgical discussion; jaundice; tumours of the colon; diseases of the rectum, including tumours; intestinal obstruction; diverticulitis; colitis, amoebiasis, functional disturbances of the colon including mucous colitis; Hirschsprung's disease; lymphogranulomata; clinical methods and differential diagnosis; technique of the gastrointestinal series; laboratory examinations.*

The profession generally is invited to attend. A complete program and registration blank may be secured by addressing: Dr. Frederick P. Reynolds, the New York Academy of Medicine, 2 East 103rd Street, New York City.

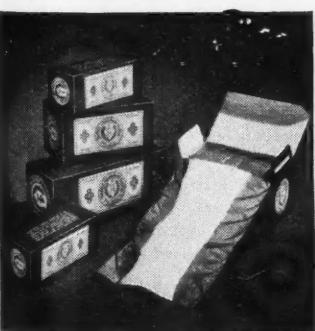
**The Legion Award Citation to William and Charles Mayo.**—The citation by the American Legion of Drs. William J. and Charles H. Mayo for distinguished public service, with the award made by the President of the United States in person, is a great honour for American medicine. It has been said that opportunities and great occasions make men. An exception to this rule is presented in the work and life of these distinguished medical leaders. They have made a small village one of the notable medical centres of the world wholly through a genius for surgery and for medical leadership. Throughout their careers they have devoted themselves to the advancement of organized medicine. The medical society of the county in which they practice was founded by their father. Both have been presidents of the American Medical Association. In 1906, when Dr. William J. Mayo delivered his presidential address to the American Medical Association, he forecast and considered some of the hazards that concern medical practice today. He attacked the abuse of medical care by public service corporations, and the abuses of public charity and of private institutions by those able to pay, and he condemned all systems of hospital and medical care dominated by laymen. He concluded his address with a plea for harmony in the medical profession, recognizing that only a strongly united opinion could gain for medicine the place in our civilization which it merits.—J. Am. M. Ass.



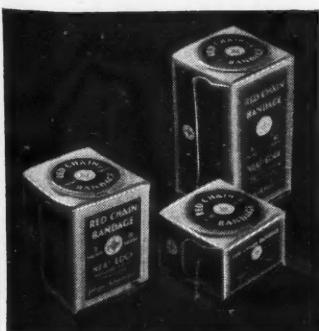
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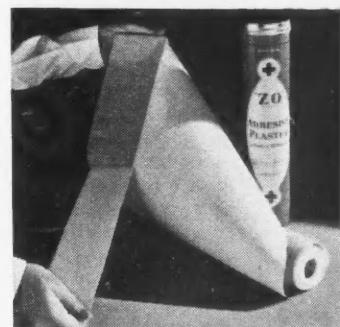
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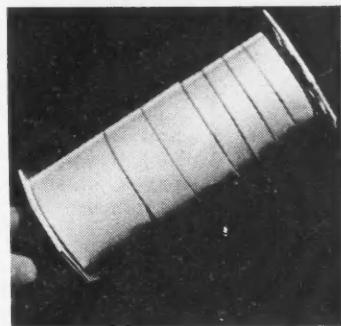
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## Book Reviews

### **Intercortical Systems of the Human Cerebrum.**

Joshua Rosett, Assistant Professor of Neurology, Columbia University. 135 pages, illustrated. Price \$3.00. Columbia University Press, New York, 1933.

As the title indicates this is a monograph dealing with the intricate problem of the subcortical and intercortical fibre-connections of the human cerebral cortex. The approach to this study has been made with the aid of a new and ingenious technique for the display of these short and complicated pathways. A description of the technique for the complete preparation of specimens for study is given in detail in the second chapter. To the novice the technique appears rather difficult and tedious, but in the hands of the author it has yielded further convincing information regarding these tracts and, incidentally, cerebral fissuration. The sixth to the thirteenth chapters, inclusive, contain in turn brief accounts of the intercortical systems as found with the author's technique in the various areas of the cortex, and many findings are of interest. Chapters three, four and five, introductory in character, are very brief, discussing questions in respect to the limitations of the technique and the author's views regarding the cell origin of the intercortical systems in general, and an explanation concerning annexant convolutions. The author felt it premature in the present work, however, to attempt a correlation of "the course and direction of any of the numerous intercortical pathways mapped out with any of the cortical cell areas delineated by any of the investigators of that subject." The final chapter is principally a discussion of the general pattern of the subcortical pathways of the fissures, and an hypothesis is propounded with regard to the cause of fissuration built on the new observations of the present work, which, in the light of the authoritative literature there reviewed, is very plausible.

This has been a painstaking work and the author deserves credit. The text is, for the most part, clearly written. The volume is not a textbook, and is of interest and of practical importance to those particularly interested in this special part of neuroanatomy and of neurophysiology. It should broaden the viewpoint of those interested in neurology, epilepsy and psychology.

[NOTE: This corrected review replaces the one which appeared in the July issue of the *Journal*, p. 116.]

**Operative Gynecology.** Dr. H. v. Peham, Privy Counsellor, Prof. of Obstetrics and Gynaecology, and Dr. J. Amreich, Privat-dozent for Obstetrics and Gynaecology, of University of Vienna. 779 pages, illustrated. Price \$26.00 (2 vols.). J. B. Lippincott, Philadelphia, Montreal and London, 1934.

This monumental work by the late Dr. H. v. Peham and his former assistant, Dr. J. Amreich, is now made available to a wider circle of readers by the enterprise of the J. B. Lippincott Company. The translation into English has been well done by Dr. L. Kraer Ferguson, Associate in Surgery at the University of Pennsylvania. It is difficult to speak of this work other than in superlative terms, so thorough, full, and explicit is it. Indeed its very thoroughness and fullness lay it open to the charge of being verbose, but every good teacher knows the value of iteration and reiteration, sometimes even of the apparently obvious. The senior intern looking forward to gynaecology as a career will be fortunate if he is in possession of this book, while the gynaecological specialist will find much to interest and instruct him in the clear and precise teaching of v. Peham which embodies the results of much original anatomical, clinical and operative research. The 467 illustrations, mostly in colour, are beyond praise. Almost all of them are original and are the work of the artist, Karl

Hajek. Those of the special part were nearly all drawn from life at actual operations.

Part I of the first volume deals with General Principles, Anæsthesia (particularly local anæsthesia), Post-operative Complications and their Prevention, Incisions and Pre- and Post-operative Treatment. Part II, dealing with gynaecological anatomy, is particularly good and will appeal to the professional anatomist as well as to the gynaecologist. The second volume treats of the operative treatment of gynaecological diseases. The various steps of operative procedure, pictured with a wealth of illustrations, appeal to the eye, and the insistence of the authors of the importance of the anatomical basis of operations leaves on the mind of the reader an impression that these operations have been evolved by a process of logical and orderly thinking. The place and value of irradiation in the therapy of carcinoma, functional uterine bleeding, and myoma are discussed.

**The Dermatergoses or Occupational Affections of the Skin.** R. Prosser White, M.D., M.B., C.M. Ed., M.R.C.S., Late President, the Certifying Factory Surgeons' Association. Fourth edition, 716 pages, illustrated. Price 35/- net. H. K. Lewis, London, 1934.

The complexity of modern living conditions is well indicated by the variety of occupational diseases. The present book is concerned with only a portion of these, namely, those affecting the skin. To describe these Dr. White coined the term "dermatergose" (literally, skin diseases from work), for as he points out some word must be found to cover not only eczemas, (which Unna used in several occupational disorders) but dermal conditions from microbial, traumatic, toxic, allergic, idiopathic and psychopathic sources. There are hypertrophies and atrophies; friction effects; plant eczemas; folliculitis from pitch, tar, paraffin and oil; warts, cancers, granulomata, etc. A single agent, such as chrome, or lime, may produce changes varying from a pale pink erythema to a pulsating sore, from a deep crack to a deep hole.

Armed with this comprehensive term Dr. White proceeds to assemble a most extraordinary collection of facts and writings relating to cutaneous disorders due to occupation. There is no industry, no occupation, no substance, which may not cause trouble; from tramps with their parasite attendants, to workers in the most hazardous trades; from water, to the obvious and deadly chemicals. Truly did Dr. James remark in 1746, "Every sick person should be asked by his physician what trade is he of?"

But this is more than a collection of isolated statements. Dr. White's own experience was vast, and he has brought it all to bear on his subject. It is remarkable to find how widely the book ranges. It is quite out of the question to leave these dermatoses to the dermatologist alone. They are too closely related to questions of sensitivity, of general tissue response to injury, and in their widest application of all, to problems of public health.

This edition was only just completed by Dr. White before his death. It stands as a worthy monument to his outstanding industry and ability.

**Sterilization? Birth Control? A Book for Family Welfare and Safety.** Helen MacMurchy, C.B.E., M.D. 156 pages. Price \$1.50. Macmillan Co. of Canada, Toronto, 1934.

Doctor Helen MacMurchy is well and favourably known to the public and to the medical profession of Canada. Believing that there was a need for a compiled summary of authoritative views on the subjects of sterilization and birth control, she has proceeded to meet this need by the preparation of a volume which, in a very satisfactory manner, accomplishes the purpose.

Ten citizens out of every thousand are unable to care for themselves; three, because they are mentally

## Acute and Generalized Staphylococcal Infections

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From various sources there has been an accumulation of evidence which suggests that much of the symptomatology of acute staphylococcal infections is attributable to liberation of staphylococcus exotoxin within the body. The serious nature of such infections would appear to be due in large measure to the highly pathogenic effects of staphylococcus exotoxin upon living cells and tissues. Consequently, the use of staphylococcus antitoxin has been advocated in the treatment of acute and of generalized infections where there is evidence that *Staphylococcus pyogenes* is the causal micro-organism. (See the issues of this Journal for June, July and August, 1934.)

As prepared by methods evolved in the Connaught Laboratories, Staphylococcus Antitoxin consists of refined and concentrated globulins from the blood-serum of horses which have been immunized against pooled toxoids and toxins of several selected strains of staphylococcus. Beneficial results have followed administration of this antitoxin in ACUTE CARBUNCLE and in CELLULITIS, OSTEOMYELITIS, MENINGITIS and SEPTICAEMIA, where staphylococcus has been the infecting agent.

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defective, and another three because of mental illness. This statement leads the author to ask: "How long is it possible for any nation to last when the normal stream of national life is polluted at its source by feeble-minded who increase in double or treble the ratio of the normal?" The book is not propaganda. There are statements of fact, dealing with such subjects as legislation and methods of sterilization. Doctor MacMurchy has succeeded in presenting the subject in all its aspects, as viewed by those authorities who are far apart in their conclusions, and so the reader learns both sides of the controversy. The Encyclical Letter of Pius XI on *Christian Marriage*, is quoted, which expresses disapproval of sterilization, as well as the Report of the Departmental Committee (Brock Committee) of 1934, which approves sterilization as the only certain method of preventing procreation. As to birth control, the book emphasizes that there is no certain means known to prevent conception if sexual intercourse occurs.

Doctor MacMurchy's views on sterilization are against compulsory action, but she is favourable to voluntary sterilization with adequate safeguards, keeping in mind that segregation in institutions will always be necessary for a large number of cases. Birth control should not, in the author's opinion, be undertaken except for definite medical reasons, and yet, there are cases needing counsel, for whom help in the way of instruction concerning birth control should be given.

The reader will be surprised to find how much solid material is packed into this small volume, which in itself is an adequate presentation, and for those who may wish to read more, the references of sources will be of value. This book is recommended without hesitation to all who have interest in the subject.

**Survey of Public Health Nursing.** By the National Organization for Public Health Nursing. Katharine Tucker, General Director. 262 pages. Price \$2.00. Commonwealth Fund, New York, 1934.

The foreword by Livingston Farrand explains the survey in these words: "It is a commonplace in the commercial world that an inventory of stock is essential to profitable operation. . . . In other words, devotion and enthusiasm can never be safely relied upon as substitutes for an accurate knowledge of values."

There are approximately 5,000 organizations in the United States employing nearly 20,000 nurses giving public health nursing service. The National Organization for Public Health Nursing, organized in 1912, promoted this self-survey to answer certain questions covering standards of service, the adequacy of these standards, to what extent they are put into practice, the whys and wherefores of variations from the standard. Twenty-eight cities, towns and counties were selected and studied as being representative of the whole country. It was found that public health nursing is administered by two official bodies—departments of health and boards of education—and by non-official bodies. The former are fewer in number, but employ the larger number of nurses. The Committee advocate that, for the immediate future, a standard of two agencies, one official and one non-official, should be accepted. The ratio of public health nurse to population is usually 1 to 3,000 or 4,000. The distribution has no relationship to need or capacity to support. Only one-third of the nurses have had any theoretical preparation through post-graduate courses, and only 7 per cent have completed an accredited public health nursing course. The preparation of nurses for public health work is a major problem, and the Committee consider, as a major recommendation, that all public health nursing agencies should provide facilities for educational supervision and for a continuous staff educational program. It is also advised that all schools of nursing incorporate the fundamental theory and experience essential for the building of further public

health nursing preparation. As to quality of service, the educational services are weakest, due likely to lack of preparation, for, as the survey points out, good educational service cannot be looked for unless the nurse knows what and how to teach.

There are practical suggestions concerning organization, the rotation of officers to avoid static control, better cooperation with the local medical society and other local organizations. All told, the report is an honest review of conditions that exist, with a frank facing of deficiencies and courageous planning for the future. From this and other surveys, it appears that the nursing profession has a firm belief in the value of self-analysis, and is not at all afraid to allow others to know the facts. It is from such constructive work that results may be looked for with assurance.

**Chronic Nasal Sinusitis and Its Relation to General Medicine.** Patrick Watson-Williams, Hon. Consulting Surgeon in Diseases of Ear, Nose and Throat, Bristol Royal Infirmary. Second edition, 262 pages, illustrated. Price \$4.50. John Wright & Sons, Bristol; Macmillan Co., Toronto, 1933.

This book is not a textbook on the diseases of the nasal accessory sinuses so much as a discussion of nasal accessory sinus disease in medical conditions. The descriptions of various radical operative proceedings, ordinary methods of examination, anatomical description, and special methods are omitted.

The novice will be much intrigued by the amazingly hopeful prognosis he will be tempted to give in many chronic ailments. The paragraph on the futility of indiscriminate operation consists of a dozen lines only. It would have enhanced the usefulness of the book to have directed the same number of pages to the subject. The book is particularly useful in that it draws special attention to some refinements of nasal examination and diagnosis. It should be read by all senior students in oto-laryngology, and by internists with a broad background of experience. Dr. Watson-Williams' enthusiasm for his subject, really his life study, has gained for him a high place in the study of disease of the accessory sinuses. If he has been carried away a little, and has placed accessory sinus sepsis (without occult pus), too prominently in the etiology of many obscure cases in general medicine, it is only a natural error and one readily forgiven.

**Clinical Studies on the Physiology of the Eye.** J. Grandson Byrne, M.A., M.D. 144 pages, illustrated. Price 10s. 6d. H. K. Lewis, London, 1934.

This book consists in part of a summary of recent work by the same author entitled "Studies on the Physiology of the Eye" and in part an application of his theory of the mechanisms governing palpebral, pupillary and lenticular movements to explain various clinical conditions. Chapters 1 to 8 summarize his earlier work. Chapter 10 deals with the mechanism of the Argyll-Robertson pupil, where he quotes earlier workers who found lesions (1) between the optic tract and the constrictor centre; (2) in the ciliary ganglion; (3) in the cervical spinal cord; and (4) in the cervical sympathetic nerve, and then states that various types of the Argyll-Robertson pupil are found, which vary in size and shape and which show paradoxical dilatation or constriction or pseudoparadoxical dilatation in a positive or negative phase. These variations, according to Byrne, prove that lesions in (1) involve the afferent dilator and constrictor paths; in (2) the efferent constrictor paths; in (3) the afferent constrictor paths; and in (4) the efferent dilator paths. In support of these views he mentions that retinal illumination always elicits a preliminary dilatation of the pupil, and that there is no such thing as accommodation without convergence. The book ends with a chapter on the treatment of the disorders of accommodation, in which he states that too many

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bifocal glasses are worn, that the constant wearing of glasses for astigmatism is a mistake, and that the maintenance of efficient accommodation depends upon the daily natural exercise of the external ocular muscles. This view opposes the fundamental views of refraction and accommodation in the various types of ametropia.

**Benign Tumours in the Third Ventricle of the Brain: Diagnosis and Treatment.** Walter E. Dandy, M.D., Adjunct Professor of Surgery, Johns Hopkins University. 171 pages, illustrated. Price \$5.00. Charles C. Thomas, Springfield, and Baltimore, 1933.

This is a clinical monograph concerning so-called benign third ventricle tumours. For descriptive purposes the author has divided these into two groups: (1) colloid cysts, and (2) a heterogenous group of apparently benign tumours. He presents 21 such, all of which were removed surgically.

After a general introduction, the second chapter consists of case reports on the 5 colloid cysts. In each instance a clear, brief, clinical history is given followed by notes on the positive neurological and x-ray findings. Stress is laid on ventriculography in these cases and remarks upon ventriculographic interpretation offered. A full account of the surgical procedure adopted in each case is given and post-operative notes added. At the end the tumour is grossly described and, rather too briefly, notes on the microscopic examination are appended. In section three his series of primary benign tumours is similarly treated.

Section four is devoted to a statistical and descriptive analysis of symptoms and signs, diagnosis, pathology and treatment. Considerable space is given to the discussion of headache, intermittency of symptoms, dizziness, loss of vision, weakness and numbness of extremities and other findings. Some paragraphs are devoted to the question of metabolic, endocrine, sympathetic and sleep disturbances and to x-ray diagnosis. Observations of interest are those concerned with loss of hearing for high tones as tested with the audiometer. Several paragraphs are given to questions relative to the diagnostic surgical procedures, *i.e.*, ventriculography, ventricular estimation, and encephalography, and to the operative approach itself, followed by a summary of the gross and microscopic pathological findings, while section five consists of a list of forty leading papers on the subject.

The clinical histories and operative notes are well arranged, clearly written and instructive. The microscopic descriptions, when present, are inadequate, but are aided by good illustrations. The facts of clinical analysis are interesting and useful. The book will be useful to students, neurologists and neurosurgeons and those interested in problems connected with tumours of the third ventricle and disturbances of that region.

**Neurology.** Roy R. Grinker, Associate Professor of Neurology, University of Chicago. 979 pages, illustrated. Price \$8.50. C. C. Thomas, Springfield, Ill., and Baltimore, Md., 1933.

The first half of this book deals quite extensively with questions of development, anatomy, physiology, and pathology, clinically applied; the second half deals more specifically with disease of the nervous system. Chapter 17 deals quite fully with the important question of brain tumours, their pathology, general localizing, and x-ray methods of diagnosis and treatment. Arterial encephalography is not favoured by the author, however; more recently Professor Moniz has used thorotrust with apparent greater safety. Chapter 19 reviews the diseases of the cerebro-spinal vascular system. Inflammatory disease and the primary infections of the central nervous system follow in Chapters 20 and 21, respectively; the latter includes the virus diseases, multiple sclerosis, the encephalomyelitides and myelitides and diffuse sclerosis. Chapter

22 is devoted to the question of syphilis. Spinal, head, and birth trauma are dealt with in Chapter 23. The question of post-traumatic sequelæ and their treatment is considered and the author gives his opinion which is at variance with some other authorities on the subject.

Succeeding chapters take up "The Atrophies", "The Epilepsies", including theoretical considerations regarding the nature of epilepsy, "Headaches", "Blood Dyscrasias and Deficiency Diseases". The modern conceptions regarding the relation between vitamin deficiency and the blood dyscrasias are discussed to some extent, and the modern treatment of pernicious anaemia included. Final chapters concern the question of "Exogenous Toxins and noxious Agents Affecting the Nervous System", the "Degenerative Diseases" and the problem of "Developmental Defects".

As a textbook of neurology this is an excellent work, correlating in lucid style physiological, anatomical and embryological fundamentals with the clinical data. It is a correlation of structure and function with clinical neurology, bringing in at all times the more modern conceptions and more recently discovered facts. The author expresses his own opinion rather forcibly at times on controversial points, but this does not detract from the text. The book can be highly recommended as a text of neurology. It is well printed and the illustrations are excellent. It contains 979 pages.

**System of Clinical Medicine.** Thomas D. Savill, M.D. Ninth edition edited by Agnes Savill, M.D., and E. C. Warner, M.D. 1063 pages, illustrated. Price \$9.25. Ed. Arnold & Co., London; Macmillan Co., Toronto, 1933.

The ninth edition of this familiar textbook is welcomed by the profession. Unchanged in its general scheme, it has been thoroughly brought up to date by adding notes on recent advances in medicine. The list of contributors remains the same, with the exception of Dr. Redvers Ironsides who has succeeded Dr. Harry Campbell. Dr. Ironsides has revised considerably the chapter on nervous diseases. A few new illustrations add materially to the charm of the book. As before, our readers will find the book useful and trustworthy.

#### BOOKS RECEIVED

**Infantilism.** E. Apert, Physician to Hospital for Sick Children, Paris. Translated by R. W. B. Ellis, M.D., 117 pages, illustrated. Price \$2.50. Martin Hopkinson, Ltd., London; McAinch & Co., Toronto, 1933.

**Pink Disease (Infantile Acrodynia).** Ch. Rocaz, Physician-in-Chief, L'Hospice des Enfants Assisés, Bordeaux. Translated by Ian J. Wood, M.D., 153 pages, illustrated. Price \$2.50. Martin Hopkinson, Ltd., London; McAinch & Co., Toronto, 1933.

**Medical Annual, 1934.** A year book of Treatment and Practitioner's Index. 642 pages, illustrated. Price \$6.00. John Wright & Sons, Bristol; Macmillan Co., Toronto.

**Aids to Obstetrics.** Leslie Williams, M.D., M.S., F.R.C.S., M.C.O.G., Obstetric Surgeon to Out-Patients, St. Mary's Hospital. Tenth edition, 219 pages. Price \$1.15. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1934.

**Aids to Operative Surgery.** Cecil P. G. Wakeley, D.Sc., F.R.C.S., F.R.S., Senior Surgeon, King's College Hospital. Second edition, 225 pages. Price \$1.15. Baillière, Tindall & Cox, London; Macmillan Co., Toronto, 1934.